WEST Search History

DATE: Tuesday April 16, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L25	((class adj I) near empty) same (bead$4 or sepharose$4)	0	L25
L24	((class adj I) near empty) near (bead$4 or sepharose$4)	0	L24
L23	((class adj I) near empty) same immobiliz$5	0	L23
L22	((class adj I) nearempty) same immobiliz$5	50	L22
L21	((class adj I) same empty) same immobiliz$5	0	L21
L20	((class adj I) same empty) same (bead$4 or matrix or support) same immobiliz$5	0	L20
L19	((class adj I) same empty) same (bead$4 or matrix or support)	7	L19
L18	((class adj I) near empty) same (bead$4 or matrix or support)	1	L18
L17	((class adj I) near empty) near (bead$4 or matrix or support)	0	L17
L16	((class adj I)near empty) near (bead$4 or matrix or support)	0	L16
L15	(class adj I) and (bead$4 or matrix or support)	3616	L15
L14	L9 and (bead$4 or matrix or support)	165	L14
L13	L9 and bead$4	91	L13
L12	L10.clm	33	L12
L11	L10 and clm	0	L11
L10	L9 and empty	33	L10
L9	L8 and mhc	230	L9
L8	(luxemburg)[IN] OR (jackson)[IN] or (Peter) [in]	187832	L8
L7	(luxemburg)[IN] OR (jackson)[IN]	13287	L7
L6	(anti$thrombin adj III) and (administ?)	1	L6
L5	(antithrombin adj III) and (administ?)	1	L5
L4	(antithrombin adj III) and(administ?)	1	L4
L3	(antithrombin adj III) same (administ?)	1	L3
L2	L1 and (antithrombin adj III)	18	L2
L1	(Roemisch)[IN] OR (stauss)[IN]	169	L1

END OF SEARCH HISTORY

L17 #3, #5

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> dis his

     (FILE 'HOME' ENTERED AT 12:52:53 ON 16 APR 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 12:53:02 ON 16 APR 2002
L1         41486 S (MHC AND (CLASS (1N) I))
L2           374 S L1 AND EMPTY
L3           106 S L2 AND (SUPPORT OR MATRIX OR BEAD)
L4            82 DUP REM L3 (24 DUPLICATES REMOVED)
L5         24364 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER ?/AU
L6          7162 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER P?/AU
L7             8 S L6 AND (MHC AND EMPTY)
L8             5 DUP REM L7 (3 DUPLICATES REMOVED)
L9             5 S L2 AND (BEAD OR SEPHAROSE)
L10            2 DUP REM L9 (3 DUPLICATES REMOVED)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      82.40      82.61

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -4.34      -4.34

STN INTERNATIONAL LOGOFF AT 13:09:26 ON 16 APR 2002
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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS  3  Jan 25  Searching with the P indicator for Preparations
 NEWS  4  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  5  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  6  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  7  Mar 08  Gene Names now available in BIOSIS
 NEWS  8  Mar 22  TOXLIT no longer available
 NEWS  9  Mar 22  TRCTHERMO no longer available
 NEWS 10  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 11  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 12  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
 NEWS 13  Apr 08  "Ask CAS" for self-help around the clock
 NEWS 14  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 15  Apr 09  ZDB will be removed from STN

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 12:52:53 ON 16 APR 2002

=> file medline caplus embase biosis
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 12:53:02 ON 16 APR 2002

FILE 'CAPLUS' ENTERED AT 12:53:02 ON 16 APR 2002
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FILE 'BIOSIS' ENTERED AT 12:53:02 ON 16 APR 2002
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=> s (MHC and (class (1N) I))
L1       41486 (MHC AND (CLASS (1N) I))

=> s l1 and empty
L2         374 L1 AND EMPTY

=> s l2 and (support or matrix or bead)
L3         106 L2 AND (SUPPORT OR MATRIX OR BEAD)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4          82 DUP REM L3 (24 DUPLICATES REMOVED)

=> dis l4 1-82 ibib abs

L4   ANSWER 1 OF 82     MEDLINE
ACCESSION NUMBER:   2002094214     MEDLINE
DOCUMENT NUMBER:    21681656   PubMed ID: 11823478
TITLE:              Cutting edge: Tapasin is retained in the endoplasmic
                    reticulum by dynamic clustering and exclusion from
                    endoplasmic reticulum exit sites.
AUTHOR:             Pentcheva Tsvetelina; Spiliotis Elias T; Edidin Michael
CORPORATE SOURCE:   Department of Biology, The Johns Hopkins University,
                    Baltimore, MD 21218, USA.
CONTRACT NUMBER:    AI 14584 (NIAID)
SOURCE:             JOURNAL OF IMMUNOLOGY, (2002 Feb 15) 168 (4) 1538-41.
                    Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        200203
ENTRY DATE:         Entered STN: 20020202
                    Last Updated on STN: 20020305
                    Entered Medline: 20020304
AB   Tapasin retains empty or suboptimally loaded MHC
     class I molecules in the endoplasmic reticulum (ER).
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However, the molecular mechanism of this process and how tapasin itself is retained in the ER are unknown. These questions were addressed by tagging tapasin with the cyan fluorescent protein or yellow fluorescent protein (YFP) and probing the distribution and mobility of the tagged proteins. YFP-tapasin molecules were functional and could be isolated in association with TAP, as reported for native tapasin. YFP-tapasin was excluded from ER exit sites even after accumulation of secretory cargo due to disrupted anterograde traffic. Almost all tapasin molecules were clustered, and these clusters diffused freely in the ER. Tapasin oligomers appear to be retained by the failure of the export machinery to recognize them as cargo.

L4 ANSWER 2 OF 82 MEDLINE
ACCESSION NUMBER: 2001545080 MEDLINE
DOCUMENT NUMBER: 21145837 PubMed ID: 11248071
TITLE: Ligand-independent assembly of recombinant human CD1 by using oxidative refolding chromatography.
COMMENT: Comment in: Proc Natl Acad Sci U S A. 2001 Mar 13;98(6):2950-2
AUTHOR: Altamirano M M; Woolfson A; Donda A; Shamshiev A; Briseno-Roa L; Foster N W; Veprintsev D B; De Libero G; Fersht A R; Milstein C
CORPORATE SOURCE: Centre for Protein Engineering, Hills Road, Cambridge CB2 2QH, United Kingdom.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Mar 13) 98 (6) 3288-93. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011011
Last Updated on STN: 20020121
Entered Medline: 20011204
AB CD1 is an **MHC class** I-like antigen-presenting molecule consisting of a heavy chain and beta(2)-microglobulin light chain. The in vitro refolding of synthetic **MHC class** I molecules has always required the presence of ligand. We report here the use of a folding method using an immobilized chaperone fragment, a protein disulphide isomerase, and a peptidyl-prolyl cis-trans isomerase (oxidative refolding chromatography) for the fast and efficient assembly of ligand-free and ligand-associated CD1a and CD1b, starting with material synthesized in Escherichia coli. The results suggest that "**empty**" **MHC class** I-like molecules can assemble and remain stable at physiological temperatures in the absence of ligand. The use of oxidative refolding chromatography thus is extended to encompass complex multisubunit proteins and specifically to members of the extensive, functionally diverse and important immunoglobulin supergene family of proteins, including those for which a ligand has yet to be identified.

L4 ANSWER 3 OF 82 MEDLINE
ACCESSION NUMBER: 2001481732 MEDLINE
DOCUMENT NUMBER: 21400823 PubMed ID: 11509592
TITLE: Exogenous peptides presented by transporter associated with antigen processing (TAP)-deficient and TAP-competent cells: intracellular loading and kinetics of presentation.
AUTHOR: Luft T; Rizkalla M; Tai T Y; Chen Q; MacFarlan R I; Davis I D; Maraskovsky E; Cebon J
CORPORATE SOURCE: Melbourne Tumor Biology Branch, Ludwig Institute for Cancer Research, Austin and Repatriation Medical Centre, Heidelberg, Victoria, Australia.. Thomas_Luft@med.uni-heidelberg.de
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Sep 1) 167 (5) 2529-37. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010830
Last Updated on STN: 20020122
Entered Medline: 20011205
AB This study investigates the differential capacity of TAP-deficient T2 cells, TAP-competent EBV cells, and immature and mature dendritic cells to present peptides to preformed CTL lines. It demonstrates that presentation of exogenous peptides involves peptide uptake and loading onto newly synthesized **MHC class** I molecules. This mechanism was best demonstrated for low affinity peptides in the presence of irrelevant peptides competing for HLA binding sites. Under these circumstances, inhibition of protein synthesis with cycloheximide or vesicular trafficking with brefeldin A significantly reduced the presentation of low affinity peptides. This was not restored by adding exogenous beta(2)-microglobulin to stabilize the **MHC** complex on the cell surface. In contrast, presentation of high affinity peptides was not sensitive to cycloheximide or brefeldin A, which suggests that different mechanisms may operate for presentation of high and low affinity peptides by TAP-competent cells. High affinity peptides can apparently compete with peptides in preloaded **MHC class** I molecules at the cell surface, whereas low affinity peptides require **empty MHC** molecules within cells. Accordingly, very high concentrations of exogenous low affinity peptides in conjunction with active **MHC class** I metabolism were required to allow successful presentation against a background of competing intracellular high affinity peptides in TAP-competent cells. These findings have implications for the design of peptide and protein-based vaccines.

L4 ANSWER 4 OF 82 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001455926 MEDLINE
DOCUMENT NUMBER: 21382449 PubMed ID: 11489993
TITLE: Tapasin enhances peptide-induced expression of H2-M3 molecules, but is not required for the retention of open conformers.
AUTHOR: Lybarger L; Yu Y Y; Chun T; Wang C R; Grandea A G 3rd; Van Kaer L; Hansen T H
CORPORATE SOURCE: Department of Genetics, Washington University School of Medicine, St. Louis, MO 63110, USA.
CONTRACT NUMBER: AI07163 (NIAID)
AI19867 (NIAID)
AI42793 (NIAID)
AI46553 (NIAID)

SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Aug 15) 167 (4) 2097-105.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010815
Last Updated on STN: 20020121
Entered Medline: 20011205

AB H2-M3 is a class Ib MHC molecule that binds a highly restricted pool of peptides, resulting in its intracellular retention under normal conditions. However, addition of exogenous M3 ligands induces its escape from the endoplasmic reticulum (ER) and, ultimately, its expression at the cell surface. These features of M3 make it a powerful and novel model system to study the potentially interrelated functions of the ER-resident class I chaperone tapasin. The functions ascribed to tapasin include: 1) ER retention of peptide-empty class I molecules, 2) TAP stabilization resulting in increased peptide transport, 3) direct facilitation of peptide binding by class I, and 4) peptide editing. We report in this study that M3 is associated with the peptide-loading complex and that incubation of live cells with M3 ligands dramatically decreased this association. Furthermore, high levels of open conformers of M3 were efficiently retained intracellularly in tapasin-deficient cells, and addition of exogenous M3 ligands resulted in substantial surface induction that was enhanced by coexpression of either membrane-bound or soluble tapasin. Thus, in the case of M3, tapasin directly facilitates intracellular peptide binding, but is not required for intracellular retention of open conformers. As an alternative approach to define unique aspects of M3 biosynthesis, M3 was expressed in human cell lines that lack an M3 ortholog, but support expression of murine class Ia molecules. Unexpectedly, peptide-induced surface expression of M3 was observed in only one of two cell lines. These results demonstrate that M3 expression is dependent on a unique factor compared with class Ia molecules.

L4 ANSWER 5 OF 82 MEDLINE
ACCESSION NUMBER: 2001430663 MEDLINE
DOCUMENT NUMBER: 21359540 PubMed ID: 11466371
TITLE: Functional roles of TAP and tapasin in the assembly of M3-N-formylated peptide complexes.
AUTHOR: Chun T; Grandea A G 3rd; Lybarger L; Forman J; Van Kaer L; Wang C R
CORPORATE SOURCE: Gwen Knapp Center for Lupus and Immunology Research, Committee on Immunology and Department of Pathology, University of Chicago, 924 East 57th Street, Chicago, IL 60637, USA.
CONTRACT NUMBER: AI40310 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Aug 1) 167 (3) 1507-14.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011029
Last Updated on STN: 20011029
Entered Medline: 20011025

AB H2-M3 is a MHC class Ib molecule with a high propensity to bind N-formylated peptides. Due to the paucity of endogenous Ag, the majority of M3 is retained in the endoplasmic reticulum (ER). Upon addition of exogenous N-formylated peptides, M3 trafficks rapidly to the cell surface. To understand the mechanism underlying Ag presentation by M3, we examined the role of molecular chaperones in M3 assembly, particularly TAP and tapasin. M3-specific CTLs fail to recognize cells isolated from both TAP-deficient (TAP(o)) and tapasin-deficient mice, suggesting that TAP and tapasin are required for M3-restricted Ag presentation. Impaired M3 expression in TAP(o) mice is due to instability of the intracellular pool of M3. Addition of N-formylated peptides to TAP(o) cells stabilizes M3 in the ER and partially restores surface expression. Surprisingly, significant amounts of M3 are retained in the ER in tapasin-deficient mice, even in the presence of N-formylated peptides. Our results define the role of TAP and tapasin in the assembly of M3-peptide complexes. TAP is essential for stabilization of M3 in the ER, whereas tapasin is critical for loading of N-formylated peptides onto the intracellular pool of M3. However, neither TAP nor tapasin is required for ER retention of empty M3.

L4 ANSWER 6 OF 82 MEDLINE
ACCESSION NUMBER: 2002017925 MEDLINE
DOCUMENT NUMBER: 21337287 PubMed ID: 11444385
TITLE: Accessory proteins that control the assembly of MHC molecules with peptides.
AUTHOR: Van Kaer L
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN 37232-0295, USA.. luc.vankaer@mcmail.vanderbilt.edu
SOURCE: IMMUNOLOGIC RESEARCH, (2001) 23 (2-3) 205-14. Ref: 39
Journal code: 8611087. ISSN: 0257-277X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020124
Entered Medline: 20011231

AB The stable assembly of Major Histocompatibility Complex (MHC) molecules with peptides is controlled by a number of cofactors, including proteins with general housekeeping functions and proteins with dedicated functions in MHC assembly. Recent work in my laboratory has focused on two chaperones, tapasin (tpn) and DM, that play critical roles in the loading of peptides onto MHC class I and MHC class II molecules, respectively. Tapasin is a transmembrane protein that tethers empty class I molecules in the endoplasmic reticulum to the transporter associated with antigen processing. DM is a peptide exchange factor that binds with empty and peptide-loaded class II molecules in endosomal and lysosomal compartments. Although a number of different functions for tapasin and DM have been proposed, emerging evidence suggests that both of these chaperones retain unstable MHC

molecules in peptide-loading compartments until they bind with high-affinity peptides. These cofactors therefore promote the surface expression of long-lived **MHC**-peptide complexes.

L4 ANSWER 7 OF 82 MEDLINE
ACCESSION NUMBER: 2001188188 MEDLINE
DOCUMENT NUMBER: 21174472 PubMed ID: 11274924
TITLE: Tapasin: an ER chaperone that controls **MHC class I** assembly with peptide.
AUTHOR: Grandea A G 3rd; Van Kaer L
CORPORATE SOURCE: Howard Hughes Medical Institute, Dept of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, TN 37232-0295, USA.
SOURCE: Trends Immunol, (2001 Apr) 22 (4) 194-9. Ref: 43
Journal code: DZX; 100966032. ISSN: 1471-4906.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705
AB The stable assembly of **MHC class I** molecules with peptides in the endoplasmic reticulum (ER) involves several accessory molecules. One of these accessory molecules is tapasin, a transmembrane protein that tethers **empty class I** molecules to the peptide transporter associated with antigen processing (TAP). Here, evidence is presented that tapasin retains **class I** molecules in the ER until they acquire high-affinity peptides.

L4 ANSWER 8 OF 82 MEDLINE
ACCESSION NUMBER: 2001296024 MEDLINE
DOCUMENT NUMBER: 21275565 PubMed ID: 11380691
TITLE: Macrophages present exogenous antigens by **class I** major histocompatibility complex molecules via a secretory pathway as a consequence of interferon-gamma activation.
AUTHOR: Martin-Orozco N; Isibasi A; Ortiz-Navarrete V
CORPORATE SOURCE: Unidad de Investigacion Medica en Inmunoquimica, Hospital de Especialidades, Centro Medico Nacional SXXI Instituto Mexicano del Seguro Social, Mexico.
SOURCE: IMMUNOLOGY, (2001 May) 103 (1) 41-8.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628
AB Macrophages can process and present exogenous antigens on major histocompatibility complex (**MHC**) **class I** molecules through an alternative mechanism involving the internalization of antigens and the secretion of peptides loading **MHC class I** molecules at the cell surface. In this paper, we found that interferon-gamma (IFN-gamma) -activated macrophages infected with Salmonella typhimurum secreted peptides able to load **empty MHC** Kb molecules on co-cultured TAP-2-deficient RMA-S cells, added as targets for peptide loading. The increase in **class I** Kb on the RMA-S cells, resulting from the macrophage-derived peptides, exhibited a comparable stability as the direct addition of an exogenous Kb-binding peptide (OVA257-264) to the RMA-S cells. In both cases, the Kb complexes were stable for at least 3 hr after separating the RMA-S cells from the macrophages. The endosomal inhibitors, leupeptin and ammonium chloride, did not inhibit the release of peptides and the increase in Kb staining on the RMA-S cells in the co-culture systems. Brefeldin A also had no effect. P815 cells previously co-cultured with Salmonella-infected macrophages became targets for cytotoxic T lymphocytes isolated from Salmonella-infected BALB/c mice. Taken together, our data suggest that IFN-gamma-activated macrophages process exogenous antigens in an intracellular compartment where serine proteases generate peptides released to the external environment for loading **empty MHC class I** molecules at the cell surface. This TAP-independent mechanism for the **MHC class I** presentation may be involved in priming cytotoxic T lymphocytes against intracellular pathogens in vivo.

L4 ANSWER 9 OF 82 MEDLINE
ACCESSION NUMBER: 2000302792 MEDLINE
DOCUMENT NUMBER: 20302792 PubMed ID: 10843695
TITLE: The structure and stability of an HLA-A*0201/octameric tax peptide complex with an **empty** conserved peptide-N-terminal binding site.
AUTHOR: Khan A R; Baker B M; Ghosh P; Biddison W E; Wiley D C
CORPORATE SOURCE: Department of Molecular and Cellular Biology and Howard Hughes Medical Institute, Harvard University, Cambridge MA 02138, USA.
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Jun 15) 164 (12) 6398-405.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: PDB-1DUY; PDB-1DUZ
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000720
AB The crystal structure of the human **class I MHC** molecule HLA-A2 complexed with of an octameric peptide, Tax8 (LFGYPVYV), from human T cell lymphotrophic virus-1 (HTLV-1) has been determined. This structure is compared with a newly refined, higher resolution (1.8 A) structure of HLA-A2 complexed with the nonameric Tax9 peptide (LLFGYPVYV) with one more N-terminal residue. Despite the absence of a peptide residue (P1) bound in the conserved N-terminal peptide-binding pocket of the Tax8/HLA-A2 complex, the structures of the two complexes are essentially identical. Water molecules in the Tax8 complex replace the terminal amino group of the Tax9 peptide and mediate a network of hydrogen bonds among the secondary structural elements at that end of the peptide-binding

groove. Thermal denaturation measurements indicate that the Tax8 complex is much less stable, DeltaTm = 16 degrees C, than the Tax9 complex, but both can sensitize target cells for lysis by some Tax-specific CTL from HTLV-1 infected individuals. The absence of a P1 peptide residue is thus not enough to prevent formation of a "closed conformation" of the peptide-binding site. TCR affinity measurements and cytotoxic T cell assays indicate that the Tax8/HLA-A2 complex does not functionally cross-react with the A6-TCR-bearing T cell clone specific for Tax9/HLA-A2 complexes.

L4 ANSWER 10 OF 82 MEDLINE
ACCESSION NUMBER: 2000087288 MEDLINE
DOCUMENT NUMBER: 20087288 PubMed ID: 10618529
TITLE: Induction of cytotoxic T lymphocyte activity by fusion-active peptide-containing virosomes.
AUTHOR: Arkema A; Huckriede A; Schoen P; Wilschut J; Daemen T
CORPORATE SOURCE: University of Groningen, Department of Physiological Chemistry, Ant. Deusinglaan 1, 9713 AV, Groningen, Netherlands.
SOURCE: VACCINE, (2000 Jan 31) 18 (14) 1327-33. Journal code: X6O; 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000307

AB Priming of cytotoxic T lymphocyte (CTL) activity with exogenous antigen requires introduction of the antigen into the **MHC class** I presentation pathway of antigen-presenting cells. In the present study, we used fusogenic reconstituted envelopes (virosomes), derived from influenza virus, as a carrier system for delivery of a synthetic soluble peptide corresponding to a major murine CTL epitope of the influenza virus nucleoprotein (NP). Virosomes containing encapsulated NP-peptide efficiently sensitized target cells for recognition by influenza-specific CTLs generated through priming of mice with infectious virus. Intramuscular immunization of mice with peptide-containing virosomes induced a potent **class I MHC**-restricted CTL response against influenza-infected target cells. By contrast, an equal dose of NP-peptide encapsulated in fusion-inactivated virosomes did not induce CTL activity, indicating an essential role of the membrane fusion activity of the virosomes in the induction of the response. Likewise, NP-peptide encapsulated in liposomes, NP-peptide mixed with **empty** virosomes and NP-peptide in IFA failed to induce a CTL response. These results demonstrate that fusion-active virosomes represent a promising delivery system for induction of **class I MHC** -restricted CTL activity with non-replicating viral antigens.

L4 ANSWER 11 OF 82 MEDLINE
ACCESSION NUMBER: 2000175670 MEDLINE
DOCUMENT NUMBER: 20175670 PubMed ID: 10709070
TITLE: Adenoviral-mediated gene transfer of ICP47 inhibits major histocompatibility complex **class I** expression on vascular cells in vitro.
AUTHOR: Furukawa L; Brevetti L S; Brady S E; Johnson D; Ma M; Welling T H; Messina L M
CORPORATE SOURCE: University of California, San Francisco, CA 94143-0222, USA.
CONTRACT NUMBER: RO1-HL51184-04 (NHLBI)
SOURCE: JOURNAL OF VASCULAR SURGERY, (2000 Mar) 31 (3) 558-66. Journal code: KD2; 8407742. ISSN: 0741-5214.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000425

AB PURPOSE: Many viruses have evolved mechanisms to evade detection by the host immune system. The herpes simplex gene ICP47 encodes a protein that binds to the host antigen-processing transporter, inhibiting the formation of major histocompatibility complex **class I** (**MHC**-I) antigens in infected cells. **MHC**-I antigen expression is also important in acute allograft rejection. This study was designed to quantitate the effect of adenoviral-mediated gene transfer of ICP47 on **MHC**-I cell surface expression of human vascular cells. We hypothesized that the transduction of vascular cells with a replication-incompetent adenoviral vector that was expressing ICP47 (AdICP47) would inhibit constitutive and inducible **MHC**-I expression and thereby reduce the rate of cytolysis of ICP47-transduced vascular cells by sensitized cytotoxic T lymphocytes (CTL). METHODS: A replication-incompetent adenoviral vector, AdICP47, was created to express ICP47 driven by the cytomegalovirus immediate early promoter. Cultured human vascular endothelial and smooth muscle cells and human dermal fibroblasts were transduced with either AdICP47 or the control **empty** vector AddlE1. Cell surface constitutive and gamma-interferon-induced **MHC**-I expression were quantitated by flow cytometry. A standard 4-hour chromium release cytotoxicity assay was used to determine the percent cytolysis of transduced and nontransduced endothelial cells by sensitized CTL. Finally, to quantitate the specificity of the effect of ICP47 on **MHC**-I expression, adhesion molecule expression was quantitated in both transduced and nontransduced cells. RESULTS: Constitutive **MHC**-I expression in AdICP47-transduced endothelial cells was inhibited by a mean of 84% +/- 5% (SEM) in five experiments. After 48 hours of exposure to gamma-interferon, AdICP47-transduced cells exhibited a mean of 66% +/- 8% lower **MHC** -I expression than nontransduced cells. Similar inhibition in **MHC** -I expression was achieved in AdICP47-transduced vascular smooth muscle cells and dermal fibroblasts. Percent cytolysis of AdICP47-transduced endothelial cells by CTL was reduced by 72%. Finally, the specificity of the effect of transduction of ICP47 on vascular cell **MHC**-I expression was confirmed by a lack of significant change in either constitutive or tumor necrosis factor-induced vascular cell adhesion molecule/intercellular adhesion molecule expression. CONCLUSION: Transduction of vascular cells with AdICP47 strongly inhibits both constitutive and inducible **MHC**-I expression in human vascular cells. AdICP47-transduced cells exhibited a substantial reduction in cytolysis by CTL. Thus AdICP47 transduction holds promise as a technique to characterize the role of **MHC**-I expression in acute vascular allograft rejection in vivo and as a potential therapeutic intervention.

L4 ANSWER 12 OF 82 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001057695 MEDLINE
DOCUMENT NUMBER: 20484087 PubMed ID: 11027816
TITLE: Introduction of the haemagglutinin transmembrane region in the influenza virus **matrix** protein facilitates its incorporation into ISCOM and activation of specific CD8(+) cytotoxic T lymphocytes.
AUTHOR: Voeten J T; Rimmelzwaan G F; Nieuwkoop N J; Lovgren-Bengtsson K; Osterhaus A D
CORPORATE SOURCE: Institute of Virology, Who National Influenza Centre, Erasmus Medical Centre Rotterdam, The Netherlands.
SOURCE: VACCINE, (2000 Oct 15) 19 (4-5) 514-22. Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001219

AB The gene encoding the influenza virus A **matrix** (MA) protein was cloned into the bacterial expression vector pMalC with and without the sequence encoding the transmembrane region of the haemagglutinin (HA). With the resulting recombinant proteins, immune stimulating complexes (ISCOM) were prepared. The MA protein with the hydrophobic anchor region (rMAHA) associated more efficiently with ISCOM than the unmodified MA protein (rMA). A B-lymphoblastoid cell line (B-LCL) was lysed by an autologous CD8(+) cytotoxic T lymphocyte (CTL) clone specific for the MA protein after incubation with rMAHA-ISCOM but not after incubation with rMA, rMAHA, rMA-ISCOM or **empty** ISCOM. The B-LCL was also lysed by the CTL clone after incubation with **empty** ISCOM mixed with the respective MA proteins. Incubation of ISCOM with the rMAHA protein proved to be the most efficient in this respect. Addition of the proteasome inhibitors lactacystin or clasto-lactacystin beta-lactone to the B-LCL incubated with rMAHA-ISCOM or the MA proteins mixed with **empty** ISCOM dramatically decreased the lysis by the CD8(+) CTL clone. These results indicate that the addition of a hydrophobic anchor to hydrophilic proteins in combination with ISCOM facilitates their entry in the **MHC class I** processing and presentation pathway. This may be an attractive approach for the development of subunit vaccines aiming at the induction of CTL-mediated immunity.

L4 ANSWER 13 OF 82 MEDLINE
ACCESSION NUMBER: 2000181817 MEDLINE
DOCUMENT NUMBER: 20181817 PubMed ID: 10715518
TITLE: Structurally diverse forms of HLA-B27 molecules are displayed in vivo in a cell type-dependent manner.
AUTHOR: Rehm A; Rohr A; Seitz C; Wonigeit K; Ziegler A; Uchanska-Ziegler B
CORPORATE SOURCE: Transplantationslabor, Klinik fur Abdominal- und Transplantationschirurgie, Medizinische Hochschule Hannover, Hannover, Germany.
SOURCE: HUMAN IMMUNOLOGY, (2000 Apr) 61 (4) 408-18. Journal code: G9W; 8010936. ISSN: 0198-8859.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000510

AB The formation of a trimeric complex, composed of heavy chain (HC), beta(2)-microglobulin (beta(2)m) and antigenic peptide, is generally believed to be a prerequisite for the expression of HLA **class** I molecules at the cell surface in vivo. Therefore, a possible role in immunological processes for HC/beta(2)m complexes devoid of peptide has not been seriously considered. Using a novel HLA-B*2705-transgenic rat model and monoclonal antibodies that distinguish between structurally different forms of HLA-B27 molecules, we demonstrate here that **class** I molecules which appear to lack antigenic peptides are expressed in abundance on a variety of cell types in lymphoid organs. These results imply a role for structurally diverse, possibly **empty**, **MHC** molecules in physiological T cell selection which has so far not been sufficiently appreciated.

L4 ANSWER 14 OF 82 MEDLINE
ACCESSION NUMBER: 2000072762 MEDLINE
DOCUMENT NUMBER: 20072762 PubMed ID: 10605026
TITLE: HLA-F is a predominantly **empty**, intracellular, TAP-associated **MHC** class Ib protein with a restricted expression pattern.
AUTHOR: Wainwright S D; Biro P A; Holmes C H
CORPORATE SOURCE: Department of Clinical Medicine, Division of Obstetrics and Gynaecology, University of Bristol, St. Michael's Hospital, United Kingdom.
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Jan 1) 164 (1) 319-28. Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131
Last Updated on STN: 20000131
Entered Medline: 20000119

AB HLA-F is currently the most enigmatic of the human **MHC**-encoded class Ib genes. We have investigated the expression of HLA-F using a specific Ab raised against a synthetic peptide corresponding to amino acids 61-84 in the alpha1 domain of the predicted HLA-F protein. HLA-F is expressed as a beta2-microglobulin-associated, 42-kDa protein that shows a restricted tissue distribution. To date, we have detected this product only in peripheral blood B cells, B cell lines, and tissues containing B cells, in particular adult tonsil and fetal liver, a major site of B cell development. Thermostability assays suggest that HLA-F is expressed as an **empty** heterodimer devoid of peptide. Consistent with this, studies using endoglycosidase-H and cell surface immunoprecipitations also indicate that the overwhelming majority of HLA-F contains an immature oligosaccharide component and is expressed inside the cell. We have found that IFN-gamma treatment induces expression of HLA-F mRNA and HLA-F protein, but that this does not result in concomitant cell surface

expression. HLA-F associates with at least two components of the conventional **class** I assembly pathway, calreticulin and TAP. The unusual characteristics of the predicted peptide-binding groove together with the predominantly intracellular localization raise the possibility that HLA-F may be capable of binding only a restricted set of peptides.

L4 ANSWER 15 OF 82 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000072759 MEDLINE
DOCUMENT NUMBER: 20072759 PubMed ID: 10605023
TITLE: Distinct functions of tapasin revealed by polymorphism in **MHC class** I peptide loading.
AUTHOR: Peh C A; Laham N; Burrows S R; Zhu Y; McCluskey J
CORPORATE SOURCE: Department of Immunology, Allergy and Arthritis, Flinders University of South Australia, Bedford Park.
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Jan 1) 164 (1) 292-9.
Journal code: IPB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131
Last Updated on STN: 20000131
Entered Medline: 20000119
AB Peptide assembly with **class** I molecules is orchestrated by multiple chaperones including tapasin, which bridges **class** I molecules with the TAP and is critical for efficient Ag presentation. In this paper, we show that, although constitutive levels of endogenous murine tapasin apparently are sufficient to form stable and long-lived complexes between the human HLA-B*4402 (B*4402) and mouse TAP proteins, this does not result in normal peptide loading and surface expression of B*4402 molecules on mouse APC. However, increased expression of murine tapasin, but not of the human TAP proteins, does restore normal cell surface expression of B*4402 and efficient presentation of viral Ags to CTL. High levels of soluble murine tapasin, which do not bridge TAP and **class** I molecules, still restore normal surface expression of B*4402 in the tapasin-deficient human cell line 721.220. These findings indicate distinct roles for tapasin in **class** I peptide loading. First, tapasin-mediated bridging of TAP-**class** I complexes, which despite being conserved across the human-mouse species barrier, is not necessarily sufficient for peptide loading. Second, tapasin mediates a function which probably involves stabilization of **empty class** I molecules and which is sensitive to structural compatibility of components within the loading complex. These discrete functions of tapasin predict limitations to the study of HLA molecules across some polymorphic and species barriers.

L4 ANSWER 16 OF 82 MEDLINE
ACCESSION NUMBER: 2000455724 MEDLINE
DOCUMENT NUMBER: 20434843 PubMed ID: 10981964
TITLE: Impaired assembly yet normal trafficking of **MHC class** I molecules in Tapasin mutant mice.
AUTHOR: Grandea A G 3rd; Golovina T N; Hamilton S E; Sriram V; Spies T; Brutkiewicz R R; Harty J T; Eisenlohr L C; Van Kaer L
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.. grandea@mcmail.vanderbilt.edu
CONTRACT NUMBER: AI30581 (NIAID)
AI39501 (NIAID)
AI46455 (NIAID)
SOURCE: IMMUNITY, (2000 Aug) 13 (2) 213-22.
Journal code: CCF; 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000925
AB Loading of peptides onto major histocompatibility complex **class** I molecules involves a multifactorial complex that includes tapasin (TPN), a membrane protein that tethers **empty class** I glycoproteins to the transporter associated with antigen processing. To evaluate the in vivo role of TPN, we have generated Tpn mutant mice. In these animals, most **class** I molecules exit the endoplasmic reticulum (ER) in the absence of stably bound peptides. Consequently, mutant animals have defects in **class** I cell surface expression, antigen presentation, CD8+ T cell development, and immune responses. These findings reveal a critical role of TPN for ER retention of **empty class** I molecules. Tpn mutant animals should prove useful for studies on alternative antigen-processing pathways that involve post-ER peptide loading.

L4 ANSWER 17 OF 82 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000135933 MEDLINE
DOCUMENT NUMBER: 20135933 PubMed ID: 10669764
TITLE: Insect cells as HLA-restricted antigen-presenting cells for the IFN-gamma elispot assay.
AUTHOR: Janetzki S; Song P; Gupta V; Lewis J J; Houghton A N
CORPORATE SOURCE: Swim Across America Laboratory and Departments of Surgery and Medicine, Memorial Sloan-Kettering Cancer Center, New York 10021, USA.. janetzki_sylvania/mskcc_sur@mskmail.mskcc.org
CONTRACT NUMBER: CA47179 (NCI)
PO1 CA33049 (NCI)
RO156821
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (2000 Feb 3) 234 (1-2) 1-12.
Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000316

AB Measurement of specific cellular immune responses in patients undergoing immunotherapy is difficult. Established approaches, including cytotoxicity (e.g., 51Cr release) and cytokine release assays, require in vitro culturing for several weeks or more of patients' peripheral blood mononuclear cells (PBMC) and the addition of exogenous cytokines. Therefore, the immunological response does not reflect in vivo conditions. To address these disadvantages, we have used an interferon-gamma (IFN-gamma) Elispot assay for detecting peptide-specific CD8(+) lymphocytes in PBMC. A limitation of this assay is the lack of a reproducible source of antigen-presenting cells (APCs). Currently available APCs often lead to significant background levels. It has been shown that transfected insect cells can express **empty** **MHC class I** molecules on their surface. We have transfected Drosophila melanogaster S2 cells and the Lepidopteran line Sf9 with the gene encoding human HLA-A2.1. We demonstrate that insect cells expressing a human HLA molecule effectively function as APCs in the IFN-gamma Elispot assay. Initially the feasibility of the assay was assessed using CD8(+) T cells from HLA-A2.1(+) donors with known reactivity against an HLA-A2.1-binding epitope of the influenza **matrix** protein. Use of insect cells as APCs abrogated background spots, increasing sensitivity. We further observed that a short-term prestimulation of PBMC with peptide-pulsed insect cells markedly enhanced the frequency of peptide-specific T cells that could be measured in the Elispot assay without increasing the background. This approach was then used to measure CD8(+) T cell reactivity to a peptide from tyrosinase, an antigen that is processed and presented by melanoma cells. Insect cells expressing human HLA molecules provide a standard APC for monitoring CD8(+) T cell responses to tumor and viral peptides during immunotherapy.

L4 ANSWER 18 OF 82 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:795994 CAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

GB 1998-12099	A	19980606
GB 1998-13291	A	19980620
GB 1998-13611	A	19980624
GB 1998-13835	A	19980627
GB 1998-14110	A	19980701
GB 1998-14580	A	19980707
GB 1998-15438	A	19980716
GB 1998-15574	A	19980718
GB 1998-15576	A	19980718
GB 1998-16085	A	19980724
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L4 ANSWER 19 OF 82 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
GB 2339200	B2	20010912		
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

GB 1998-12098	A	19980606
GB 1998-28289	A	19981223
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819
WO 1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

DUPLICATE 5

L4 ANSWER 20 OF 82 MEDLINE

ACCESSION NUMBER:	1999441363 MEDLINE
DOCUMENT NUMBER:	99441363 PubMed ID: 10510382
TITLE:	Thermolabile H-2Kb molecules expressed by transporter associated with antigen processing-deficient RMA-S cells are occupied by low-affinity peptides.
AUTHOR:	De Silva A D; Boesteanu A; Song R; Nagy N; Harhaj E; Harding C V; Joyce S
CORPORATE SOURCE:	Department of Microbiology, Pennsylvania State University College of Medicine, Milton S. Hershey Medical Center 17033, USA.
CONTRACT NUMBER:	AI-34343 (NIAID) AI-35276 (NIAID) CA-70149 (NCI)
SOURCE:	JOURNAL OF IMMUNOLOGY, (1999 Oct 15) 163 (8) 4413-20. Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY:	United States Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:	199911
ENTRY DATE:	Entered STN: 20000111 Last Updated on STN: 20000111 Entered Medline: 19991104

AB RMA-S cells do not express functional TAP, yet they express **MHC class I** molecules at the cell surface, especially at reduced temperatures (26 degrees C). It is generally assumed that such **class I** molecules are "**empty**," devoid of any associated peptide. A radiochemical approach was used to label **class I**-associated peptides and to determine the extent to which Kb molecules in RMA-S cells are associated with peptides. These studies revealed that at 26 degrees C Kb molecules in RMA-S cells are occupied with self-peptides. Such peptides stably associate with Kb at 26 degrees C but easily dissociate from them at 37 degrees C, suggesting low-affinity interactions between Kb and the associated peptides. At 26 degrees C, at least some of these Kb molecules are stably expressed in a peptide-receptive state on the cell surface, whereas at 37 degrees C they are short lived and are only transiently capable of binding and presenting exogenously supplied OVA 257-264 peptide for presentation to CD8+ Kb-restricted T lymphocytes. Thus contrary to current models of **class I** assembly in TAP-deficient RMA-S cells, the presumably "**empty**" molecules are in fact associated with peptides at 26 degrees C. Together, our data **support** the existence of an alternative mechanism of peptide binding and display by **MHC class I** molecules in TAP-deficient cells that could explain their ability to present Ag.

L4 ANSWER 21 OF 82 MEDLINE

ACCESSION NUMBER:	2000059389 MEDLINE
DOCUMENT NUMBER:	20059389 PubMed ID: 10590255
TITLE:	Definition and transfer of a serological epitope specific for peptide-**empty** forms of **MHC class I**.
AUTHOR:	Yu Y Y; Myers N B; Hilbert C M; Harris M R; Balendiran G K; Hansen T H
CORPORATE SOURCE:	Department of Genetics, Washington University School of Medicine, St Louis, MO 63110, USA.
CONTRACT NUMBER:	AI19687 (NIAID) K08AI01498 (NIAID) T32AI07163 (NIAID)
SOURCE:	INTERNATIONAL IMMUNOLOGY, (1999 Dec) 11 (12) 1897-906. Journal code: AY5; 8916182. ISSN: 0953-8178.
PUB. COUNTRY:	ENGLAND: United Kingdom Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

AB Nascent **class** I molecules have been hypothesized to undergo a conformational change when they bind peptide based on the observation that most available antibodies only detect peptide-loaded **class** I. Furthermore recent evidence suggests that this peptide-facilitated conformational change induces the release of **class** I from association with transporter associated with antigen processing (TAP)/tapasin and other endoplasmic reticulum proteins facilitating **class** I assembly. To learn more about the structure of peptide-**empty class** I , we have studied mAb 64-3-7 that is specific for peptide-**empty** forms of L(d). We show here that mAb 64-3-7 detects a linear stretch of amino acids including principally residues 48Q and 50P. Furthermore, we demonstrate that the 64-3-7 epitope can be transferred to other **class** I molecules with limited mutagenesis. Interestingly, in the folded **class** I molecule residues 48 and 50 are on a loop connecting a beta strand (under the bound peptide) with the alpha(1) helix (rising above the ligand binding site). Thus it is attractive to propose that this loop is a hinge region. Importantly, the three-dimensional structure of this loop is strikingly conserved among **class** I molecules. Thus our findings suggest that all **class** I molecules undergo a similar conformational change in the loop around residues 48 and 50 when they associate with peptide.

L4 ANSWER 22 OF 82 MEDLINE
ACCESSION NUMBER: 1999282778 MEDLINE
DOCUMENT NUMBER: 99282778 PubMed ID: 10354367
TITLE: Alloreactive cytotoxic T-cell function, peptide nonspecific.
AUTHOR: Mullbacher A; Lobigs M; Kos F J; Langman R
CORPORATE SOURCE: Division of Immunology and Cell Biology, John Curtin School of Medical Research, Australian National University, Australia.
CONTRACT NUMBER: RR07716 (NCRR)
SOURCE: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1999 Jun) 49 (6) 563-9.
Journal code: UCW; 0323767. ISSN: 0300-9475.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990713

AB The recognition requirements necessary for murine alloreactive cytotoxic T-cells to carry out their effector function has been investigated using target cells that express a unique **class** I major histocompatibility complex (**MHC**)-peptide pair. The human cell line T2 and the murine cell line RMA-S are defective in peptide transport components needed to effectively express stable **MHC** **class** I molecules at the cell surface. When T2 cells were infected with a vaccinia virus that encoded the Kd gene and provided with a Kd-motif peptide from the nucleoprotein of influenza virus (NPP), these cells could be lysed by polyclonal allo Kd-reactive cytotoxic T-lymphocytes (CTL). Similar results were obtained with the murine RMA-S-Kd cell line, transfected with cDNA able to express some ' **empty**' Kd that is heat-labile. Adding another Kd-motif peptide from influenza virus haemagglutinin (HAP) stabilized the surface expression of Kd and allowed the RMA-S-Kd cells to be lysed before or after heat shock. At 27 degrees C anti-Kd alloreactive CTL-lysed target cells in the presence and absence of HAP peptide. Alloreactive CTL appear to have a more stringent requirement for a high density of **MHC** **class** I on cell surfaces relative to peptide-specific **MHC**-restricted CTL. We conclude that while Kd-restricted CTL activity is strictly peptide-specific, anti-Kd-specific alloreactivity is **MHC** allele-specific, but peptide-nonspecific. This conclusion is at odds with the Standard Model of T-cell receptor (TCR) function, but consistent with the predictions of a Competing Model of TCR function.

L4 ANSWER 23 OF 82 MEDLINE
ACCESSION NUMBER: 1999161832 MEDLINE
DOCUMENT NUMBER: 99161832 PubMed ID: 10064069
TITLE: Cell surface expression of HLA-E: interaction with human beta2-microglobulin and allelic differences.
AUTHOR: Ulbrecht M; Couturier A; Martinozzi S; Pla M; Srivastava R; Peterson P A; Weiss E H
CORPORATE SOURCE: Institut fur Anthropologie und Humangenetik, Ludwig-Maximillians-Universitat Munchen, Germany.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1999 Feb) 29 (2) 537-47.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990316

AB The formation of a trimeric complex composed of **MHC** **class** I heavy chain, beta2-microglobulin (beta2m) and peptide ligand is a prerequisite for its efficient transport to the cell surface. We have previously demonstrated impaired intracellular transport of the human class Ib molecule HLA-E in mouse myeloma X63 cells cotransfected with the genes for HLA-E and human beta2m (hbeta2m), which is most likely attributable to inefficient intracellular peptide loading of the HLA-E molecule. Here we demonstrate that cell surface expression of HLA-E in mouse cells strictly depends on the coexpression of hbeta2m and that soluble **empty** complexes of HLA-E and hbeta2m display a low degree of thermostability. Both observations imply that low affinity interaction of HLA-E with beta2m accounts to a considerable extent for the observed low degree of peptide uptake in the endoplasmic reticulum. Moreover, we show that the only allelic variation present in the caucasoid population located at amino acid position 107 (Gly or Arg) greatly affects intracellular transport and cell surface expression upon transfection of the respective alleles into mouse cells. No obvious difference was found with regard to the sequence of the peptide ligand.

L4 ANSWER 24 OF 82 MEDLINE
ACCESSION NUMBER: 1999401153 MEDLINE
DOCUMENT NUMBER: 99401153 PubMed ID: 10469918
TITLE: Positively charged liposome functions as an efficient immunoadjuvant in inducing cell-mediated immune response to soluble proteins.
AUTHOR: Nakanishi T; Kunisawa J; Hayashi A; Tsutsumi Y; Kubo K; Nakagawa S; Nakanishi M; Tanaka K; Mayumi T
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Osaka University, 1-6, Yamadaoka, Suita, Osaka, Japan.
SOURCE: JOURNAL OF CONTROLLED RELEASE, (1999 Aug 27) 61 (1-2) 233-40.
Journal code: C46; 8607908. ISSN: 0168-3659.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991013

AB In order to design an optimized liposome immunoadjuvant for inducing cell-mediated immune response against soluble proteinaceous antigens, we investigated the effect of liposomal surface charge on the immunoadjuvant action. Positively charged liposomes containing soluble antigens functioned as a more potent inducer of antigen-specific cytotoxic T lymphocyte responses and delayed type hypersensitivity response than negatively charged and neutral liposomes containing the same concentrations of antigens. To clarify the reason of the differential immune response, we examined the delivery of soluble proteins by the liposomes into the cytoplasm of macrophages, using fragment A of diphtheria toxin (DTA) as a marker. We found that positively charged liposomes encapsulating DTA are cytotoxic to macrophages, while **empty** positively charged liposomes, DTA in negatively charged and neutral liposomes are not. Consistent with this, only macrophages pulsed with OVA in positively charged liposomes could significantly stimulate OVA-specific, **class I MHC**-restricted T cell hybridoma. These results suggest that the positively charged liposomes can deliver proteinaceous antigens efficiently into the cytoplasm of the macrophages/antigen-presenting cells, where the antigens are processed to be presented by **class I MHC** molecules to induce the cell-mediated immune response. Possible development of the safe and effective vaccine is discussed.

L4 ANSWER 25 OF 82 MEDLINE
ACCESSION NUMBER: 1998438533 MEDLINE
DOCUMENT NUMBER: 98438533 PubMed ID: 9765288
TITLE: Secondary structure composition and pH-dependent conformational changes of soluble recombinant HLA-DM.
AUTHOR: Busch R; Reich Z; Zaller D M; Sloan V; Mellins E D
CORPORATE SOURCE: Department of Pediatrics, Stanford University, Stanford, California 94305, USA.. rbushch@leland.stanford.edu
CONTRACT NUMBER: AI-28809 (NIAID)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Oct 16) 273 (42) 27557-64.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981106

AB HLA-DM catalyzes the release of invariant chain fragments from newly synthesized major histocompatibility complex (**MHC**) class II molecules, stabilizes **empty** class II molecules, and edits class II-associated peptides by preferentially releasing those that are loosely bound. The ability of HLA-DM to carry out these functions in vitro is pH dependent, with an optimum at pH 4.5-5.5 and poor activity at pH 7. The structural basis for these properties of HLA-DM is unknown. Sequence homology suggests that HLA-DM resembles classical, peptide-binding **MHC** class II molecules. In this study, we examined whether HLA-DM has a secondary structure composition consistent with an **MHC** fold and whether HLA-DM changes conformation between pH 5 and pH 7. Far-UV circular dichroism (CD) spectra of recombinant soluble HLA-DM (sDM) indicate that HLA-DM belongs to the alpha/beta class of proteins and structurally resembles both **MHC class I** and **class** II molecules. The CD peak around 198 nm increases upon going from neutral to endosomal pH and drops sharply upon denaturation below pH 3.5, distinguishing at least three states of sDM: the denatured state and two highly similar folded states. Fluorescence emission spectra show a slight blue-shift and a approximately 20% drop in intensity at pH 5 compared with pH 7. Unfolding experiments using guanidinium chloride show that the stability of sDM is somewhat reduced but not lost at pH 5. These results indicate that sDM undergoes a pH-dependent conformational change between neutral and endosomal pH. The change seems to involve both hydrogen bonding patterns and the hydrophobic core of sDM and may contribute to the pH dependence of DM activity.

L4 ANSWER 26 OF 82 MEDLINE
ACCESSION NUMBER: 1998233686 MEDLINE
DOCUMENT NUMBER: 98233686 PubMed ID: 9574542
TITLE: Interaction of HLA-E with peptides and the peptide transporter in vitro: implications for its function in antigen presentation.
AUTHOR: Ulbrecht M; Modrow S; Srivastava R; Peterson P A; Weiss E H
CORPORATE SOURCE: Institut fur Anthropologie und Humangenetik, Ludwig-Maximilians-Universitat Munchen, Munich, Germany.
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 May 1) 160 (9) 4375-85.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 20000303
Entered Medline: 19980521

AB The assembly of **MHC** Ia molecules in the endoplasmic reticulum requires the presence of peptide ligands and beta2m and is facilitated by chaperones in an ordered sequence of molecular interactions. A crucial

step in this process is the interaction of the **class I** alpha-chain/beta2m dimer with TAP, which is believed to ensure effective peptide loading of the **empty class I** molecule. We have previously demonstrated impaired intracellular transport of the class Ib molecule HLA-E in mouse myeloma cells cotransfected with the genes for HLA-E and human beta2m, which is most likely attributable to inefficient intracellular peptide loading of the HLA-E molecule. We therefore analyzed the ability of HLA-E in the transfectant cell line to bind synthetic peptides by means of their ability to enhance cell surface expression of HLA-E. Peptide binding was confirmed by testing the effect on the thermostability of soluble **empty** HLA-E/human beta2m dimers. Two viral peptides binding to HLA-E were thus identified, for which the exact positioning of the N terminus appeared critical for binding, whereas the contribution of the length of the C terminus seemed to be minor, allowing peptides as short as seven amino acids and up to 16 amino acids to exhibit considerable binding activity. Furthermore, we demonstrate that HLA-E interacts with TAP and that this interaction can be prolonged by the proteasome inhibitor N-acetyl-L-leucyl-L-leucyl-L-norleucinal, which reduces the intracellular peptide pool. The presented data indicate that HLA-E is capable of presenting peptide ligands similar to the repertoire of HLA class Ia molecules.

L4 ANSWER 27 OF 82 MEDLINE
ACCESSION NUMBER: 1998334027 MEDLINE
DOCUMENT NUMBER: 98334027 PubMed ID: 9670952
TITLE: NK cells can recognize different forms of **class I MHC**.
AUTHOR: Su R C; Kung S K; Gariepy J; Barber B H; Miller R G
CORPORATE SOURCE: Department of Medical Biophysics, Ontario Cancer Institute, University of Toronto, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Jul 15) 161 (2) 755-66. Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980811
Last Updated on STN: 19990129
Entered Medline: 19980730
AB NK recognition and lysis of targets are mediated by activation receptor(s) whose effects may be over-ridden by inhibitory receptors recognizing **class I MHC** on the target. Incubation of normal lymphoblasts with a peptide that can bind to their **class I MHC** renders them sensitive to lysis by syngeneic NK cells. By binding to **class I MHC**, the peptide alters or masks the target structure recognized by an inhibitory NK receptor(s). This target structure is most likely an "**empty**" dimer of **class I** heavy chain and beta2m as opposed to a "full" **class I** trimer formed by binding of specific peptide that is recognized by CTL.

L4 ANSWER 28 OF 82 MEDLINE
ACCESSION NUMBER: 1998124484 MEDLINE
DOCUMENT NUMBER: 98124484 PubMed ID: 9464837
TITLE: Processing of exogenous hepatitis B surface antigen particles for Ld-restricted epitope presentation depends on exogenous beta2-microglobulin.
AUTHOR: Schirmbeck R; Thoma S; Reimann J
CORPORATE SOURCE: Institute for Medical Microbiology and Immunology, University of Ulm, Germany.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Dec) 27 (12) 3471-84. Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980220
AB Processing of exogenous hepatitis B surface antigen (HBsAg) particles in an endolysosomal compartment generates peptides that bind to the major histocompatibility complex (**MHC**) **class I** molecule Ld and are presented to CD8+ cytotoxic T lymphocytes. Surface-associated '**empty**' **MHC class I** molecules associated neither with peptide, nor with beta2-microglobulin (beta2m) are involved in this alternative processing pathway of exogenous antigen for **MHC class I** -restricted peptide presentation. Here, we demonstrate that internalization of exogenous beta2m is required for endolysosomal generation of presentation-competent, trimeric Ld molecules in cells pulsed with exogenous HBsAg. These data point to a role of endocytosed exogenous beta2m in the endolysosomal assembly of **MHC class I** molecules that present peptides from endosomally processed, exogenous antigen.

L4 ANSWER 29 OF 82 MEDLINE
ACCESSION NUMBER: 97225981 MEDLINE
DOCUMENT NUMBER: 97225981 PubMed ID: 9122223
TITLE: Stability of **empty** and peptide-loaded class II major histocompatibility complex molecules at neutral and endosomal pH: comparison to **class I** proteins.
AUTHOR: Reich Z; Altman J D; Boniface J J; Lyons D S; Kozono H; Ogg G; Morgan C; Davis M M
CORPORATE SOURCE: Department of Microbiology and Immunology, Stanford University School of Medicine, CA 94305-5402, USA.
CONTRACT NUMBER: AI 19512 (NIAID)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Mar 18) 94 (6) 2495-500. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970424
AB The structure and thermal stability of **empty** and peptide-filled forms of the murine class II major histocompatibility complex (**MHC**) molecule I-E(k) were studied at neutral and mildly acidic pH. The two

forms have distinct circular dichroic spectra, suggesting that a conformational change may accompany peptide binding. Thermal stability profiles indicate that binding of peptide significantly increases the thermal stability of the **empty** heterodimers at both neutral and mildly acidic pH. Free energies calculated from these data provide a direct measure of this stabilization and show that the **empty** form of I-E(k) is significantly more stable than that of **class I MHC** proteins. Furthermore, for the two **MHC** class II proteins that were analyzed (I-E(k) and I-A(d)), thermal stability was not significantly altered by acidification. In contrast, of four **class I MHC** molecules studied, three have shown a significant loss in complex stability at low pH. The marked stability exhibited by their **empty** form, as well as their resistance to low pH, as observed in this study, correlate well with the ability of class II **MHC** molecules to traverse and bind peptides in acidic endosomal vesicles.

L4 ANSWER 30 OF 82 MEDLINE
ACCESSION NUMBER: 97454415 MEDLINE
DOCUMENT NUMBER: 97454415 PubMed ID: 9310490
TITLE: Downregulation of TAP1 in B lymphocytes by cellular and Epstein-Barr virus-encoded interleukin-10.
AUTHOR: Zeidler R; Eissner G; Meissner P; Uebel S; Tampe R; Lazis S; Hammerschmidt W
CORPORATE SOURCE: GSF-National Research Center for Environment and Health, Institut fur Klinische Molekularbiologie und Tumorgenetik, Munchen, Germany.
CONTRACT NUMBER: CA70723 (NCI)
SOURCE: BLOOD, (1997 Sep 15) 90 (6) 2390-7.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971020

AB Virally infected cells degrade intracellular viral proteins proteolytically and present the resulting peptides in association with major histocompatibility complex (**MHC**) **class I** molecules to CD8+ cytotoxic T lymphocytes (CTLs). These cells are normally prone to CTL-mediated elimination. However, several viruses have evolved strategies to avoid detection by the immune system that interfere with the pathway of antigen presentation. Epstein-Barr virus (EBV) expresses a predominantly late protein, the BCRF1 gene product vIL-10, that is similar in sequence to the human interleukin-10 (hIL-10). We show here that vIL-10 affects the expression of one of the two transporter proteins (TAPs) associated with antigen presentation. Similarly, hIL-10 showed the same activity. Expression of the LMP2 and TAP1 genes but not expression of TAP2 or LMP7 is efficiently downregulated, indicating a specific IL-10 effect on the two divergently transcribed TAP1 and LMP2 genes. Downregulation of TAP1 by IL-10 hampers the transport of peptide antigens into the endoplasmatic reticulum, as shown in the TAP-specific peptide transporter assay, their loading onto **empty MHC** I molecules, and the subsequent translocation to the cell surface. As a consequence, IL-10 causes a general reduction of surface **MHC** I molecules on B lymphocytes that might also affect the recognition of EBV-infected cells by cytotoxic T cells.

L4 ANSWER 31 OF 82 MEDLINE
ACCESSION NUMBER: 97296310 MEDLINE
DOCUMENT NUMBER: 97296310 PubMed ID: 9151894
TITLE: The active site of ICP47, a herpes simplex virus-encoded inhibitor of the major histocompatibility complex (**MHC**)-encoded peptide transporter associated with antigen processing (TAP), maps to the NH2-terminal 35 residues.
AUTHOR: Galocha B; Hill A; Barnett B C; Dolan A; Raimondi A; Cook R F; Brunner J; McGeoch D J; Ploegh H L
CORPORATE SOURCE: Center for Cancer Research, Department of Biology, Massachusetts Institute of Technology, Cambridge 02139, USA.
CONTRACT NUMBER: RO1AI33456 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1997 May 5) 185 (9) 1565-72.
Journal code: I2V; 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970602

AB The herpes simplex virus (HSV) immediate early protein ICP47 inhibits the transporter associated with antigen processing (TAP)-dependent peptide translocation. As a consequence, **empty** major histocompatibility complex (**MHC**) **class I** molecules are retained in the endoplasmic reticulum and recognition of HSV-infected cells by cytotoxic T lymphocytes is abolished. We chemically synthesized full-length ICP47 (sICP47) and show that sICP47 inhibits TAP-dependent peptide translocation in human cells. Its biological activity is indistinguishable from that of recombinant ICP47 (rICP47). By using synthetic peptides, we mapped the core sequence of ICP47 minimally required for TAP inhibition to residues 2-35. This segment is located within the region of the molecule conserved between ICP47 from HSV-1 and HSV-2. Through alanine scanning substitution we identified three segments within this region that are critical for the ability to inhibit TAP function. The interaction of ICP47 with TAP is unlikely to mimic precisely that of the transported peptides, as deduced from differential labeling of the TAP1 and TAP2 subunits using sICP47 fragments with chemical cross-linkers.

L4 ANSWER 32 OF 82 MEDLINE
ACCESSION NUMBER: 97166078 MEDLINE
DOCUMENT NUMBER: 97166078 PubMed ID: 9013971
TITLE: IFN regulatory factor-1 gene transfer into an aggressive, nonimmunogenic sarcoma suppresses the malignant phenotype and enhances immunogenicity in syngeneic mice.
AUTHOR: Yim J H; Wu S J; Casey M J; Norton J A; Doherty G M
CORPORATE SOURCE: Laboratory of Biological Therapy, Department of Surgery, Washington University School of Medicine, St. Louis, MO

63110, USA.
CONTRACT NUMBER: 5T32 CA-09621 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGY, (1997 Feb 1) 158 (3) 1284-92.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970219

AB IFN-gamma has a direct antitumor effect on many tumor cell lines mediated through the IFN-gammaR. One effect of IFN-gamma is to induce the nuclear transcription factor IFN regulatory factor-1 (IRF-1), which may function as a tumor suppressor. In this study, mouse IRF-1 cDNA under a high constitutive expression promoter was transfected into the highly aggressive, nonimmunogenic MCA 101 murine sarcoma. Clones were obtained by G418 selection and screened for IRF-1 mRNA expression by reverse transcriptase-PCR (RT-PCR). High expression clones had high levels of two MHC class I proteins (H-2Kb and H-2Db) on the cell surface that correlated with increased levels of class I mRNA by RT-PCR. Furthermore, these clones also had increased levels of MHC class II protein (I-Ab), which correlated with increased levels of one subunit of class II mRNA by RT-PCR. IRF-1-expressing clones had markedly diminished cell growth in vitro and decreased anchorage-independent growth in a soft agar assay. These clones also demonstrated markedly prolonged tumor latency and slowed growth in syngeneic C57BL/6 mice. IRF-1 gene-transfected cells had shortened tumor latency and formed faster growing tumors in gamma-irradiated immunodeficient mice compared with results in immunocompetent mice. Mice immunized with IRF-1-transfected cells were protected against subsequent challenge with IRF-1 transfected cells and also demonstrated greater tumor latency and slower tumor growth against subsequent challenge with untransfected cells compared with mice immunized with empty vector-transfected cells. These studies demonstrate a tumor suppressor effect of IRF-1, which acts in vivo through both partial reversion of the malignant phenotype and enhanced immune recognition and may play a role in the antitumor effects of IFN-gamma.

L4 ANSWER 33 OF 82 MEDLINE
ACCESSION NUMBER: 97303796 MEDLINE
DOCUMENT NUMBER: 97303796 PubMed ID: 9160098
TITLE: MHC class I presentation of live and heat-inactivated Sendai virus antigen in T2Kb cells depends on an intracellular compartment with endosomal characteristics.
AUTHOR: Liu T; Zhou X; Abdel-Motal U M; Ljunggren H G; Jondal M
CORPORATE SOURCE: Microbiology and Tumor Biology Center, Karolinska Institute, Stockholm, Sweden.
SOURCE: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1997 May) 45 (5), 527-33.
Journal code: UCW; 0323767. ISSN: 0300-9475.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970620
Last Updated on STN: 19970620
Entered Medline: 19970612

AB T2Kb cells, which do not express TAP1/2 peptide transporters or the low molecular weight protein 2/7 (LMP2/7) proteasomal subunits, can still process and present both live and heat-inactivated Sendai virus (SV). As this operation may also reflect the existence of an alternative processing pathway in normal antigen-presenting cells (APC), the authors have characterized it using intracellular inhibitors and anti-Kb monoclonal antibodies (MoAbs). From the results with lipophilic amines (ammonium chloride, methylamine and chloroquine), cytoskeletal inhibitors (cytochalasin B and vinblastine), and an endoprotease inhibitor (phenylmethylsulfonyl fluoride, PMSF), the authors conclude that the processing of SV antigen in T2Kb cells has endosomal characteristics depending on cellular activities such as uptake, vesicular transport and intracellular-vesicular proteolysis. In addition, internalized 'empty' Kb molecules derived from the T2Kb cell surface appeared to be involved in the presentation of SV antigen, as demonstrated by a protocol using a combination of the Golgi inhibitor brefeldin A(BFA) and anti-Kb antibodies. The results thus indicate that T2Kb cells process SV antigen in an endosomal-like compartment which contain recycling 'empty' Kb molecules.

L4 ANSWER 34 OF 82 MEDLINE
ACCESSION NUMBER: 1998107720 MEDLINE
DOCUMENT NUMBER: 98107720 PubMed ID: 9448031
TITLE: An improved assembly assay for peptide binding to HLA-B*2705 and H-2K(k) class I MHC molecules.
AUTHOR: Tan L; Andersen M H; Elliott T; Haurum J S
CORPORATE SOURCE: The Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford, UK.
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1997 Nov 10) 209 (1) 25-36.
Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980224
Last Updated on STN: 19980224
Entered Medline: 19980206

AB The assembly assay for peptide binding to class I major histocompatibility complex (MHC) is based on the ability to stabilise MHC class I molecules from mutant cell lines by the addition of suitable peptides. Such cell lines lack a functional transporter associated with antigen presentation (TAP) and as a result accumulate empty, unstable class I molecules in the ER. These dissociate rapidly in cell lysates unless they are stabilised by the addition of an appropriate binding peptide during lysis. The extent of stabilisation of class I molecules is directly related to the binding affinity of the added peptide. However, some MHC class I molecules, including HLA-B * 2705 and H-2Kk are unusually stable in their

peptide-receptive state making them inappropriate for analysis using this assay or assays which depend on the ability of peptides to stabilise **MHC class I** molecules at the cell surface.
Here we present an improved method that permits reliable measurements of peptide binding to such **class I MHC**
molecules that are unusually stable in the absence of peptide. Cells are lysed in the presence of peptide and incubated at 4 degrees C. After 2 h, during which peptide binding to **empty MHC** molecules
occurs, the lysate is heated to a temperature which preferentially destabilises those **MHC** molecules that remain **empty**. We
have used this technique to assay peptide binding to HLA-B * 2705, as well as to the murine allele H-2Kk which also displays a stable phenotype when transfected into TAP-deficient T2 cells and show that this method represents a marked improvement over previous methods in terms of lower background signal and higher recovery of peptide bound molecules.

L4 ANSWER 35 OF 82 MEDLINE
ACCESSION NUMBER: 97098106 MEDLINE
DOCUMENT NUMBER: 97098106 PubMed ID: 8942647
TITLE: Peptide interaction with a **class I** major histocompatibility complex-encoded molecule: allosteric control of the ternary complex stability.
AUTHOR: Gakamsky D M; Bjorkman P J; Pecht I
CORPORATE SOURCE: Department of Immunology, Weizmann Institute of Science, Rehovot, Israel.. lidima@wis.weizmann.ac.il
SOURCE: BIOCHEMISTRY, (1996 Nov 26) 35 (47) 14841-8. Journal code: A0G; 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970102

AB Thermodynamics and kinetics of interaction between a soluble **class I MHC** heterodimer composed of the H-2Kd heavy chain (H)
and human beta 2microglobulin (beta 2m) with a dansylated peptide series based on residues 147-155 of influenza virus nucleoprotein sequence were studied by means of real-time fluorescence measurements.
Peptide-heterodimer binding is a second-order process with specific rates practically independent of peptide structure (3-5 x 10(6) M-1 s-1). The ternary complex assembly involves a rate-limiting step of beta 2m association with H to yield an unstable heterodimer (tau < or = 5 s, 37 degrees C). Peptide binding provides a positive feedback enhancing H's affinity for beta 2m, thus stabilizing the ternary complex. The latter decays by either peptide or beta 2m dissociation. The first-order rate constants of peptide dissociation (0.5 x 10(-2))-(0.4 x 10(-3)) s-1, 37 degrees C) depend on their structures and are faster than that of beta 2m dissociation. The former process decreases the H affinity for beta 2m and induces their dissociation. This dissociation, in turn, drastically lowers H affinity for peptide. Thus, these three components produce a system which is stable as a trimer. This behavior is rationalized by the functional requirements of **class I** molecules: Peptide
structure determines the ternary complex's lifetime, and peptide rebinding on the cell surface is rendered unlikely by the limited stability of the **empty** heterodimers and the very low peptide affinity of the heavy chains.

L4 ANSWER 36 OF 82 MEDLINE
ACCESSION NUMBER: 97030275 MEDLINE
DOCUMENT NUMBER: 97030275 PubMed ID: 8876216
TITLE: The natural killer cell receptor Ly-49A recognizes a peptide-induced conformational determinant on its major histocompatibility complex **class I** ligand.
AUTHOR: Orihuela M; Margulies D H; Yokoyama W M
CORPORATE SOURCE: Department of Medicine and Pathology, Washington University School of Medicine, St. Louis, MO 63110, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Oct 15) 93 (21) 11792-7. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204

AB Natural killer (NK) cells are inhibited from killing cellular targets by major histocompatibility complex (**MHC**) **class I**
molecules. In the mouse, this can be mediated by the Ly-49A NK cell receptor that specifically binds the H-2Dd **MHC class**
I molecule, then inhibits NK cell activity. Previous experiments have indicated that Ly-49A recognizes the alpha 1/alpha 2 domains of **MHC class I** and that no specific **MHC**
-bound peptide appeared to be involved. We demonstrate here that alanine-substituted peptides, having only the minimal anchor motifs, stabilized H-2Dd expression and provided resistance to H-2Dd-transfected, transporter associated with processing (TAP)-deficient cells from lysis by Ly-49A+ NK cells. Peptide-induced resistance was blocked only by an mAb that binds a conformational determinant on H-2Dd. Moreover, stabilization of "**empty**" H-2Dd heavy chains by exogenous beta 2-microglobulin did not confer resistance. In contrast to data for **MHC class I**-restricted T cells that are specific for
peptides displayed **MHC** molecules, these data indicate that NK cells are specific for a peptide-induced conformational determinant, independent of specific peptide. This fundamental distinction between NK cells and T cells further implies that NK cells are sensitive only to global changes in **MHC class I** conformation
or expression, rather than to specific pathogen-encoded peptides. This is consistent with the "missing self" hypothesis, which postulates that NK cells survey tissues for normal expression of **MHC class I**.

L4 ANSWER 37 OF 82 MEDLINE
ACCESSION NUMBER: 96247635 MEDLINE
DOCUMENT NUMBER: 96247635 PubMed ID: 8666787
TITLE: pH dependence of **MHC class I** -restricted peptide presentation.
AUTHOR: Stryhn A; Pedersen L O; Romme T; Olsen A C; Nissen M H; Thorpe C J; Buus S

CORPORATE SOURCE: Institute for Medical Microbiology and Immunology, Copenhagen, Denmark.
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Jun 1) 156 (11) 4191-7. Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960819
Last Updated on STN: 19970203
Entered Medline: 19960808

AB The function of **MHC class I** molecules is to bind and present antigenic peptides to cytotoxic T cells. Here, we report that **class I**-restricted peptide presentation is strongly pH dependent. The presentation of some peptides was enhanced at acidic pH, whereas the presentation of others was inhibited. Biochemical peptide-**MHC class I** binding assays demonstrated that peptide-**MHC class I** complexes are more stable at neutral pH than at acidic pH. We suggest that acid-dependent peptide dissociation can generate **empty class I** molecules and that the resulting binding potential can be exploited by a subset of peptide-**MHC class I** combinations, in some cases leading to considerable peptide exchange. We further speculate that the relative instability of peptide-**class I** complexes under acidic conditions may affect the outcome of **class I** -restricted Ag presentation, as less stably associated peptides may dissociate from **class I** during passage of the acidic trans-Golgi network, and therefore may not be presented. Finally, our results may in part explain how endocytosed proteins can be presented by **MHC class I** molecules to cytotoxic T cells.

L4 ANSWER 38 OF 82 MEDLINE
ACCESSION NUMBER: 97131799 MEDLINE
DOCUMENT NUMBER: 97131799 PubMed ID: 8977273
TITLE: '**Empty**' Ld molecules capture peptides from endocytosed hepatitis B surface antigen particles for major histocompatibility complex **class I** -restricted presentation.
AUTHOR: Schirmbeck R; Reimann J
CORPORATE SOURCE: Institute for Medical Microbiology and Immunology, University of Ulm, Germany.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Dec) 26 (12) 2812-22. Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970204

AB Peptides recognized by CD8+ cytotoxic T lymphocytes in the context of major histocompatibility complex (**MHC**) **class I** molecules are usually derived from endogenous proteins synthesized within the cell. Exogenous 22-nm hepatitis B surface antigen (HBsAg) particles are taken up by many cells, and are processed in a novel peptide-transporter-independent, endosomal or lysosomal pathway for **class I** (Ld)-restricted epitope presentation. Here, we present evidence that '**empty**' Ld molecules derived from the cell surface are involved in presenting antigenic peptides from endocytosed HBsAg particles. Intracellular assembly of presentation-competent, trimeric Ld molecules required endocytosis of the exogenous antigen and ' **empty**' Ld molecules. These data assign a functional role to surface-associated, '**empty**' **MHC class** I molecules.

L4 ANSWER 39 OF 82 MEDLINE
ACCESSION NUMBER: 97096834 MEDLINE
DOCUMENT NUMBER: 97096834 PubMed ID: 8941680
TITLE: Induction of functional **empty class** I major histocompatibility complex glycoproteins by photoactivated 8-methoxypsoralen.
AUTHOR: Imaeda S; Felli A; Schmitt I; Chimenti S; Edelson R L
CORPORATE SOURCE: Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut 06510, USA.
CONTRACT NUMBER: 2RO1 CA43058 (NCI)
SOURCE: JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1996 Dec) 107 (6) 887-90. Journal code: IHZ; 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970114

AB CD8+ cytotoxic T lymphocytes (CTLs) bind to and selectively lyse tumor cells via T-cell receptor recognition of distinctive peptide antigens presented in the context of surface major histocompatibility complex **class I (MHC class I)** glycoproteins. Several human and experimental animal tumors express distinctive **MHC class I**-associated peptides, which can be selectively targeted by specific CD8+ CTLs. Malignant cells expressing low quantities of these peptides are poor inducers of CTL responses. Therefore, we have developed a method of externally loading increased amounts of antigenic peptides onto **MHC class** I molecules. In order to induce "**empty**" fillable **MHC class I** molecules capable of binding antigenic peptides, we exposed transformed murine T cells (RMA) to low dose (3 joules/cm2) ultraviolet A energy and 8-methoxypsoralen (100 ng per ml). Presence of "**empty**" **class** I molecules was ascertained by "meltdown" or loss of the thermodynamically unstable cold-induced "**empty**" molecules as identified by cytofluorography at 37 degrees C. Retained function of "**empty**" molecules was determined by their stabilization through addition of peptides of the correct size and sequence motif, prior to exposure to physiologic temperature.

L4 ANSWER 40 OF 82 MEDLINE
ACCESSION NUMBER: 96432831 MEDLINE

DOCUMENT NUMBER: 96432831 PubMed ID: 8805302
TITLE: Point mutations in the alpha 2 domain of HLA-A2.1 define a functionally relevant interaction with TAP.
AUTHOR: Lewis J W; Neisig A; Neefjes J; Elliott T
CORPORATE SOURCE: Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, UK.
SOURCE: CURRENT BIOLOGY, (1996 Jul 1) 6 (7) 873-83.
Journal code: B44; 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19970227
Entered Medline: 19970207

AB BACKGROUND: Glycoproteins encoded by the major histocompatibility complex **class I** region (**MHC class I**) present peptide antigens to cytotoxic T cells (CTLs). Peptides are delivered to the site of **MHC class I** assembly by the transporter associated with antigen processing (TAP), and cell lines that lack this transporter are unable to present endogenous antigens to CTLs. Although it has been shown that a fraction of newly synthesized **class I** molecules are in physical association with TAP, it is not known whether this interaction is functionally relevant, or where on the **class I** molecule the TAP binding site might be. RESULTS: C1R cells transfected with a mutant HLA-A2.1 heavy chain (HC), where threonine at position 134 in the alpha 2 domain is changed to lysine (T134K), are unable to present endogenous antigens to CTLs. We have studied the biochemistry of this mutant in C1R cells, and found that a large pool of unstable **empty class I** HC-beta 2m (beta-2 microglobulin) heterodimers exist that are rapidly transported to the cell surface. The T134K mutant seemed to bind peptide antigens and assemble with beta 2m as efficiently as wild-type HLA-A2.1. However, we show here that the inefficiency with which T134K presents intracellular antigen is associated with its inability to interact with the TAP heterodimer. CONCLUSIONS: These experiments establish that the **class I**-TAP interaction is obligatory for the presentation of peptide epitopes delivered to the endoplasmic reticulum (ER) by TAP. Wild-type HLA-A2.1 molecules in TAP-deficient cells are retained in the ER, whereas T134K is rapidly released to the cell surface, but is unstable, suggesting a role for the TAP complex as an intracellular checkpoint that only affects the release of **class I** molecules with stably bound peptide ligands.

L4 ANSWER 41 OF 82 MEDLINE
ACCESSION NUMBER: 97128074 MEDLINE
DOCUMENT NUMBER: 97128074 PubMed ID: 8972744
TITLE: **MHC class I** phenotype and function of human beta 2-microglobulin transgenic murine lymphocytes.
AUTHOR: Bjerager L; Pedersen L O; Bregenholt S; Nissen M H; Claesson M H
CORPORATE SOURCE: Department of Medical Anatomy, Panum Institute, University of Copenhagen, Denmark.
SOURCE: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1996 Dec) 44 (6) 615-22.
Journal code: UCW; 0323767. ISSN: 0300-9475.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19970116

AB Lymphoid cells from beta 2-microglobulin (beta 2m) knockout mice transgenic for human (h) beta 2m (C57BL/10 m beta 2m-/h beta 2m+) were compared with normal mice for their binding to exogenously added h beta 2m, binding to a H-2Db peptide and for functional activity in a one-way allogenic MLC. Based on data from cellular binding studies, Scatchard analyses and flow cytometry, it is concluded that exogenous h beta 2m does not bind to hybrid **MHC class I** (**MHC** -I) molecules composed of mouse heavy chain/h beta 2m molecules expressed on lymphocytes of transgenic mice. Immunoprecipitation and SDS-PAGE analysis of metabolically labelled normal C57BL/6 lymph node cells showed binding of exogenous h beta 2m to **MHC**-I, in particular, to the H-2Db molecule through an exchange with endogenous mouse beta 2m. In contrast to normal H-2Db molecules, hybrid H-2Db expressed on the surface of transgenic lymphocytes binds radiolabelled peptide in the absence of exogenous added h beta 2m suggesting that a stable fraction of hybrid H-2Db molecules is **empty** or contain peptides with very low affinity. In a one-way allogenic mixed lymphocyte culture, transgenic splenocytes were found to be far less stimulatory than normal splenocytes. In contrast, transgenic alloreactive cytotoxic T lymphocytes developed earlier in MLC than their non-transgenic counterparts. These data indicate that the hybrid mouse heavy chain/h beta 2m complex alters the alloantigenic repertoire and influences important aspects of T-cell activation.

L4 ANSWER 42 OF 82 MEDLINE
ACCESSION NUMBER: 97182840 MEDLINE
DOCUMENT NUMBER: 97182840 PubMed ID: 9030979
TITLE: External glycopeptide binding to **MHC class-I** in relation to expression of TAP transporters, beta 2-microglobulin and to pH.
AUTHOR: Abdel-Motal U M; Dahmen J; Liu T; Ljunggren H G; Jondal M
CORPORATE SOURCE: Microbiology and Tumor Biology Center (MTC), Karolinska Institute, Stockholm, Sweden.
SOURCE: IMMUNOLOGY LETTERS, (1996 Dec 1) 54 (1) 31-5.
Journal code: GIH; 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970602

AB **MHC class-I** binding glycopeptides are easily visualized on the cell surface by carbohydrate specific monoclonal antibodies. By comparing the staining intensity between anti-carbohydrate

and anti-**MHC class-I** specific monoclonal antibodies, an estimation of the fraction of peptide accessible '**empty**' sites on the cell surface of **MHC class-I** molecules can be made. This system was used to analyze glycopeptide binding to **MHC class-I** molecules in relation to transporter associated with antigen processing (TAP) peptide transporters and beta 2-M expression, using gene targeted mice, and in relation to pH. Approximately 15, 40, and 95% '**empty** ' Db molecules were found on activated T cells from normal, beta 2-M-/- and TAP -/- mice, respectively. The ASN9-6h-Gal2 glycopeptide also bound to transfected '**empty**' Db molecules on T1-Db, T2-Db and T3-Db cells with a preference for T2-Db cells, lacking TAP peptide transporters. The stability of glycopeptide binding to H-2Db is also highest on T2-Db cells. pH was found to influence binding either positively or negatively, using four different glycopeptides, binding either to Db or Kb. We conclude that external glycopeptide binding may reflect important functional properties in the **MHC class-I** system and that pH in different processing compartments might influence the expressed peptide repertoire.

L4 ANSWER 43 OF 82 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 95339875 MEDLINE
DOCUMENT NUMBER: 95339875 PubMed ID: 7614989
TITLE: The interaction of beta 2-microglobulin (beta 2m) with mouse **class I** major histocompatibility antigens and its ability to **support** peptide binding. A comparison of human and mouse beta 2m.
AUTHOR: Pedersen L O; Stryhn A; Holter T L; Etzerodt M; Gerwien J; Nissen M H; Thogersen H C; Buus S
CORPORATE SOURCE: Institute of Medical Microbiology and Immunology, University of Copenhagen, Denmark.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 Jun) 25 (6) 1609-16. Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950905
Last Updated on STN: 19950905
Entered Medline: 19950822

AB The function of major histocompatibility complex (**MHC**) **class I** molecules is to sample peptides derived from intracellular proteins and to present these peptides to CD8+ cytotoxic T lymphocytes. In this paper, biochemical assays addressing **MHC class I** binding of both peptide and beta 2-microglobulin (beta 2m) have been used to examine the assembly of the trimolecular **MHC class I**/beta 2m/peptide complex. Recombinant human beta 2m and mouse beta 2ma have been generated to compare the binding of the two beta 2m to mouse **class I** . It is frequently assumed that human beta 2m binds to mouse **class I** heavy chain with a much higher affinity than mouse beta 2m itself. We find that human beta 2m only binds to mouse **class I** heavy chain with slightly (about 3-fold) higher affinity than mouse beta 2m. In addition, we compared the effect of the two beta 2m upon peptide binding to mouse **class I**. The ability of human beta 2m to **support** peptide binding correlated well with its ability to saturate mouse **class I** heavy chains. Surprisingly, mouse beta 2m only facilitated peptide binding when mouse beta 2m was used in excess (about 20-fold) of what was needed to saturate the **class I** heavy chains. The inefficiency of mouse beta 2m to **support** peptide binding could not be attributed to a reduced affinity of mouse beta 2m/**MHC class I** complexes for peptides or to a reduction in the fraction of mouse beta 2m/**MHC class I** molecules participating in peptide binding. We have previously shown that only a minor fraction of **class I** molecules are involved in peptide binding, whereas most of **class I** molecules are involved in beta 2m binding. We propose that mouse beta 2m interacts with the minor peptide binding (i.e. the "**empty**") fraction with a lower affinity than human beta 2m does, whereas mouse and human beta 2m interact with the major peptide-occupied fraction with almost similar affinities. This would explain why mouse beta 2m is less efficient than human beta 2m in generating the peptide binding moiety, and identifies the **empty** **MHC class I** heavy chain as the molecule that binds human beta 2m preferentially.

L4 ANSWER 44 OF 82 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:381687 CAPLUS
DOCUMENT NUMBER: 122:158060
TITLE: Peptide influences the folding and intracellular transport of free major histocompatibility complex **class** I heavy chains
AUTHOR(S): Machold, Robert P.; Andree, Sofia; Kaer, Luc Van; Ljunggren, Hans-Gustaf; Ploegh, Hidde L.
CORPORATE SOURCE: Massachusetts Inst. Technol., Howard Hughes Med. Inst., Cambridge, MA, 02139, USA
SOURCE: J. Exp. Med. (1995), 181(3), 1111-22
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Class I** major histocompatibility complex mols. require both .beta.2-microglobulin (.beta.2m) and peptide for efficient intracellular transport. With the exception of H-2Db and Ld, **class I** heavy chains have not been detectable at the surface of cells lacking .beta.2m. The authors show that properly conformed **class I** heavy chains can be detected in a terminally glycosylated form indicative of cell surface expression H-2b, H-2d, and H-2s .beta.2m-/- Con A-stimulated splenocytes incubated at reduced temp. Furthermore, the authors demonstrate the presence of Kb mols. at the surface of .beta.2m-/- cells cultured at 37.degree.. The mode of assembly of **class I** mols. encompasses two major pathways: binding of peptide to preformed "**empty**" heterodimers, and binding of peptide to free heavy chains, followed by recruitment of .beta.2m. In **support** of the existence of the latter pathway, the authors provide evidence for a role of peptide in intracellular transport of free **class I** heavy chains, through anal. of Con A-stimulated splenocytes from transporter assocd. with antigen processing 1 (TAP1)-/-, .beta.2m-/-, and double-mutant TAP1/.beta.2m-/- mice.

L4 ANSWER 45 OF 82 MEDLINE
ACCESSION NUMBER: 96022632 MEDLINE

DOCUMENT NUMBER: 96022632 PubMed ID: 7578413
TITLE: Tap-1 and Tap-2 gene therapy selectively restores conformationally dependent HLA Class I expression in type I diabetic cells.
AUTHOR: Wang F; Li X; Annis B; Faustman D L
CORPORATE SOURCE: Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA.
CONTRACT NUMBER: CA52244 (NCI)
SOURCE: HUMAN GENE THERAPY, (1995 Aug) 6 (8) 1005-17.
Journal code: A12; 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951221

AB Genetic susceptibility to many autoimmune diseases, including insulin-dependent diabetes mellitus (IDDM) is statistically linked to the HLA class II region of chromosome 6. However, a distinguishing feature of patients with HLA class II-linked autoimmune disease is an abnormally low density of conformationally correct, self-peptide filled HLA **class** I molecules on the lymphocyte cell surface. The transporters associated with antigen processing (Tap-1 and Tap-2) are essential for normal **class** I expression and presentation of intracellular peptides, and these genes are located within the HLA class II region. The aims of this project were to determine if Tap genes could be implicated in the defective **class** I expression associated with IDDM by using a novel Epstein-Barr virus (EBV)-mediated gene transfer system to introduce a cloned, normal Tap-2 or Tap-1 gene into B cell lines from normal and IDDM patients and analyzing the effect on conformationally dependent **class** I expression. The results show that Tap-2 gene transfer in B cells from 40% of randomly selected IDDM patients increased expression of conformationally correct, cell-surface **class** I molecules to levels comparable with similarly treated B cells from normal control individuals. B cells from another 40% of IDDM patients responded to Tap-1 gene transfer. These effects were specific because B cells from normal individuals did not respond to Tap-1 or Tap-2 gene transfer with increased **class** I expression, and B cells from IDDM patients responding to Tap-2 gene transfer did not respond to Tap-1 gene transfer and vice versa. Thus, these complementation studies identify distinct, non-overlapping subsets of IDDM patients whose **class** I defect in B cells can be reversed by Tap-1 or Tap-2 gene transfer. The increase in **class** I expression induced by Tap gene transfer is associated with a reduction in the number of peptide-**empty class** I molecules as demonstrated by the response to exogenous peptide loading. Furthermore, the increase in self-peptide filled **class** I molecules induced by Tap gene transfer into B cells from IDDM patients is associated with restored antigen presentation to autologous T cells. These studies conclude that Tap gene dysfunctions may contribute to the defect in **class** I phenotype and antigen presentation demonstrated by IDDM patients. Defective presentation of self-peptides by antigen presenting cells can lead to the failed T cell education and tolerance to self antigens evident in IDDM. These studies functionally identify HLA class II region genes that contribute to an immunologic defect in IDDM.

L4 ANSWER 46 OF 82 MEDLINE
ACCESSION NUMBER: 95270280 MEDLINE
DOCUMENT NUMBER: 95270280 PubMed ID: 7751006
TITLE: Peptide engineering allows cytotoxic T-cell vaccination against human papilloma virus tumour antigen, E6.
AUTHOR: Lipford G B; Bauer S; Wagner H; Heeg K
CORPORATE SOURCE: Institute for Medical Microbiology, Technical University of Munich, Germany.
SOURCE: IMMUNOLOGY, (1995 Feb) 84 (2) 298-303.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19970203
Entered Medline: 19950622

AB Major histocompatibility complex (**MHC**) **class** I allele-specific binding motifs have proved useful in predicting cytotoxic T-cell epitopes from immunogenic proteins. In a search of the E6 protein from human papilloma virus type 16 utilizing the Kb binding motif, we discovered four potential binding peptides. One peptide, E6.1 (sequence 50-57, YDFAFRDL), was poor in its ability to stabilize **empty** Kb on RMA-S cells, with a t1/2 = 33 min versus 30 min for **empty** Kb. This peptide subsequently proved to be non-immunogenic upon mouse in vivo vaccination. It was hypothesized that an isoleucine for aspartate substitution at position 2 would improve Kb stabilization kinetics and therefore immunogenic potential. The engineered peptide E6.1 I2 increased the Kb t1/2 to 100 min and was immunogenic upon in vivo vaccination. Cytolytic T lymphocytes (CTL) raised with the E6.1 I2 peptide responded to cells pulsed with either the wild-type peptide or the engineered peptide, implying a blindness to the substitution. More striking, these CTL also lysed a syngeneic cell line transfected with the E6 gene, implying that the E6.1 peptide was processed and presented. These data demonstrate that subimmunogenic peptides can be engineered to improve binding kinetics, which in turn improves immunogenicity. Provided that poor binding peptides are processed, the induction threshold for CTL activation can be achieved with engineered peptides, thus allowing for the kill of wild-type target cells. This approach may prove relevant to the design of subunit vaccines to virally induced tumours.

L4 ANSWER 47 OF 82 MEDLINE
ACCESSION NUMBER: 1998005194 MEDLINE
DOCUMENT NUMBER: 98005194 PubMed ID: 9346837
TITLE: Identification and synthesis of altered peptides modulating T cell recognition of a synthetic peptide antigen.
AUTHOR: Ede N J; Chen W; McCluskey J; Jackson D C; Purcell A W
CORPORATE SOURCE: Department of Microbiology, University of Melbourne, Parkville, Australia.
SOURCE: BIOMEDICAL PEPTIDES, PROTEINS AND NUCLEIC ACIDS, (1995) 1 (4) 231-4.
Journal code: CSA; 9506699. ISSN: 1353-8616.
PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971114

AB In studies of T cell responses to synthetic peptides we have observed agonist and antagonist activities associated with contaminants identified within the parent synthesis. The synthesis of two candidate analogues implied by a peptide contaminant formed during the synthesis of La 51-58 (IMIKFNRL) has been carried out. The peptide contaminant was 17-18 Da smaller than the parent peptide consistent with a modified asparagine residue at position 6 and so we synthesised both an aspartimide and a nitrile analogue, representing cyclisation or dehydration of the asparagine residue. The candidate aspartimide and nitrile analogues both bound **empty** **MHC** **class** I molecules to form allo determinants recognised by monoclonal antibodies. These results demonstrate that altered synthetic peptides can bind **class** I **MHC** molecules and prompt caution in the use of synthetic peptides as a source of immunising antigen.

L4 ANSWER 48 OF 82 MEDLINE
ACCESSION NUMBER: 95343344 MEDLINE
DOCUMENT NUMBER: 95343344 PubMed ID: 7542403
TITLE: Peptide binding and presentation by mouse CD1.
COMMENT: Comment in: Science. 1995 Jul 14;269(5221):185-6
AUTHOR: Castano A R; Tangri S; Miller J E; Holcombe H R; Jackson M R; Huse W D; Kronenberg M; Peterson P A
CORPORATE SOURCE: Department of Immunology, La Jolla, CA 92037, USA.
SOURCE: SCIENCE, (1995 Jul 14) 269 (5221) 223-6.
Journal code: UJ7; 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950905
Last Updated on STN: 19960129
Entered Medline: 19950822

AB CD1 molecules are distantly related to the major histocompatibility complex (**MHC**) **class** I proteins. They are of unknown function. Screening random peptide phage display libraries with soluble **empty** mouse CD1 (mCD1) identified a peptide binding motif. It consists of three anchor positions occupied by aromatic or bulky hydrophobic amino acids. Equilibrium binding studies demonstrated that mCD1 binds peptides containing the appropriate motif with relatively high affinity. However, in contrast to classical **MHC** **class** I molecules, strong binding to mCD1 required relatively long peptides. Peptide-specific, mCD1-restricted T cell responses can be raised, which suggests that the findings are of immunological significance.

L4 ANSWER 49 OF 82 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 95174767 MEDLINE
DOCUMENT NUMBER: 95174767 PubMed ID: 7870065
TITLE: Evidence for an early heavy chain intermediate in the assembly of H-2Db **class** I **MHC** molecules.
AUTHOR: Cauley L S
CORPORATE SOURCE: University of California San Diego, Department of Biology, La Jolla 92093-0063.
CONTRACT NUMBER: AI32068 (NIAID)
SOURCE: MOLECULAR IMMUNOLOGY, (1995 Feb) 32 (2) 137-46.
Journal code: NG1; 7905289. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950407
Last Updated on STN: 19980206
Entered Medline: 19950327

AB Several recently proposed models for the in vivo biogenesis of **class** **I** **MHC** molecules focus on the retention of **empty** dimers as a postulated intermediate in the assembly of the complete complexes. The data presented in this study **support** a slightly different model of **class** **I** biogenesis, which includes a precursor population of H-2Db heavy chains (HCs) that is retained in the ER of murine cells prior to its association with beta-2 microglobulin (beta 2m). For this study the intracellular ratios of the subunits that comprise **class** **I** molecules have been manipulated to generate a transfected cell line which assembles only very small numbers of unstable H-2Db molecules. Immunoprecipitation experiments with this transfected cell line demonstrated that nascent beta 2m was assembled into complete H-2Db heterotrimers more rapidly than nascent H-2Db HCs by normal murine cells. These data were not consistent with the simultaneous retention of the two associated subunits (HC and beta 2m) in a pool of precursor molecules. However, a previously uncharacterized subset of immature H-2Db HCs, which were not associated with beta 2m, has been detected. These immature HCs exhibited several characteristics of a precursor to complete **class** **I** molecules and required a supply of endogenously synthesized peptides for their normal processing in vivo.

L4 ANSWER 50 OF 82 MEDLINE
ACCESSION NUMBER: 95323682 MEDLINE
DOCUMENT NUMBER: 95323682 PubMed ID: 7541307
TITLE: Binding of diverse peptides to **MHC** **class** I molecules inhibits target cell lysis by activated natural killer cells.
AUTHOR: Correa I; Raulet D H
CORPORATE SOURCE: Department of Molecular and Cell Biology, University of California, Berkeley 94720, USA.
CONTRACT NUMBER: RO1-AI35021 (NIAID)
SOURCE: IMMUNITY, (1995 Jan) 2 (1) 61-71.
Journal code: CCF; 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950822

Last Updated on STN: 19970203
Entered Medline: 19950804

AB **Class I MHC** expression by target cells inhibits lysis mediated by natural killer (NK) cells, often in an allele-specific fashion. It has been proposed that NK cell inhibitory receptors recognize complexes of **class I** molecules with specific cellular peptides that define self, displacement of which would render cells NK sensitive. By loading the mostly **empty** Dd **class I** molecules of cell lines deficient in peptide transporter molecules with synthetic or natural Dd-bound peptides, we have demonstrated specific dose-dependent inhibition of the Ly49+ subset of activated NK cells by **class I**-peptide complexes. Inhibition occurred with most if not all Dd-binding peptides, suggesting that Ly49+ NK cells recognize **class I**-peptide complexes largely independently of peptide composition. The results suggest a primary role of NK cells in the destruction of cells that have down-regulated or extinguished cell surface expression of some or all **class I** molecules.

L4 ANSWER 51 OF 82 MEDLINE
ACCESSION NUMBER: 96140778 MEDLINE
DOCUMENT NUMBER: 96140778 PubMed ID: 8551035
TITLE: Major histocompatibility complex **class I** binding glycopeptides for the estimation of '**empty**' **class I** molecules.
AUTHOR: Abdel-Motal U M; Berg L; Bengtsson M; Dahmen J; Kihlberg J; Magnusson G; Nilsson U; Jondal M
CORPORATE SOURCE: Microbiology and Tumor Biology Center (MTC), Karolinska Institutet, Stockholm, Sweden.
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1995 Dec 15) 188 (1) 21-31.
Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960306
Last Updated on STN: 19970203
Entered Medline: 19960220

AB Different forms of major histocompatibility complex (**MHC**) **class I** heavy chains are known to be expressed on the cell surface, including molecules which are functionally '**empty**'. Direct peptide binding to cells is obvious during sensitization of target cells in vitro for cytotoxic T lymphocyte killing and '**empty**' **MHC**-I molecules are comparatively abundant on TAP-1/2 peptide transporter mutant cells. In the present work we have estimated the fraction of '**empty**' **MHC class I** molecules using glycosylated peptides and cellular staining with carbohydrate specific monoclonal antibodies. Synthetic Db and Kb binding peptides were coupled at different positions with different di- or trisaccharides, using different spacing between the carbohydrate and the peptide backbone. Binding of sugar specific mAbs was compared in ELISA and cellular assays. An optimal Db binding glycopeptide was used for comparative staining with anti-Db and anti-carbohydrate monoclonal antibodies to estimate fractions of '**empty**' molecules on different T lymphoid cells. On activated normal T cells, a large fraction of Db molecules were found to be '**empty**'. The functional role of such '**empty**' **MHC class I** molecules on T cells is presently unclear. However, on antigen presenting cells they might participate in the antigen presentation process.

L4 ANSWER 52 OF 82 MEDLINE
ACCESSION NUMBER: 96087572 MEDLINE
DOCUMENT NUMBER: 96087572 PubMed ID: 8537084
TITLE: Competition inhibition of cytotoxic T-lymphocyte (CTL) lysis, a more sensitive method to identify candidate CTL epitopes than induction of antibody-detected **MHC class I** stabilization.
AUTHOR: Feltkamp M C; Vierboom M P; Toes R E; Ossendorp F; ter Schegget J; Melief C J; Kast W M
CORPORATE SOURCE: Department of Immunohematology and Blood Bank, University Hospital Leiden, The Netherlands.
SOURCE: IMMUNOLOGY LETTERS, (1995 Jul-Aug) 47 (1-2) 1-8.
Journal code: GIH; 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960221
Last Updated on STN: 19960221
Entered Medline: 19960206

AB We compared the efficiency of two commonly used cellular major histocompatibility complex (**MHC**) **class I** peptide-binding assays to identify a cytotoxic T lymphocyte (CTL) epitope-containing peptide among length variants derived from the human papilloma virus type 16 (HPV 16) oncoprotein E7. Although both assays identified the same sequence (E7 49-57) as the most efficient Db-binding peptide, the efficiency by which they did so differed markedly. In a peptide competition cytotoxicity (PCC) assay, based on inhibition of CTL lysis by competition for binding to **MHC class-I** molecules between a known CTL epitope-containing peptide and peptide of interest, E7 49-57 bound 45-fold more efficiently to Db than the second Db-binding peptide in line. In the widely used RMA-S **MHC class I** peptide-binding assay, based on peptide-induced stabilization of '**empty**' **MHC class-I** molecules at the surface of antigen-processing defective RMA-S cells, this difference was only 3 fold. Similar differences were observed when other Db-restricted CTL clones and CTL epitope-containing peptides were used in the PCC assay. The same phenomenon was observed when peptide binding affinities for H-2Kb were analyzed in both assays. We conclude that the PCC assay discriminates more efficiently between high- and low-affinity **MHC class I** binding peptides than the RMA-S assay. This observation is ascribed to the fact that peptide-**MHC class I** dissociation is an important parameter in the PCC but not the RMA-S assay.

L4 ANSWER 53 OF 82 MEDLINE
ACCESSION NUMBER: 94297032 MEDLINE
DOCUMENT NUMBER: 94297032 PubMed ID: 8025120
TITLE: Effects of peptide length and composition on binding to an **empty class I MHC**

heterodimer.
AUTHOR: Fahnestock M L; Johnson J L; Feldman R M; Tsomides T J; Mayer J; Narhi L O; Bjorkman P J
CORPORATE SOURCE: Division of Biology, California Institute of Technology, Pasadena 91125.
CONTRACT NUMBER: T32-CA09255 (NCI)
SOURCE: BIOCHEMISTRY, (1994 Jul 5) 33 (26) 8149-58.
Journal code: A0G; 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940818
Last Updated on STN: 19980206
Entered Medline: 19940805

AB **Class I** major histocompatibility complex (**MHC**) proteins present peptide antigens to T cells during the immune response against viruses. Peptides are loaded into newly synthesized **class I** heterodimers in the endoplasmic reticulum such that most or all cell surface **class I** molecules contain peptides derived from endogenous or foreign proteins. We previously reported the assembly of **empty** heterodimers of the murine **class I MHC** molecule H-2Kd, from denatured heavy and light chains from which endogenous peptides had been removed [Fahnestock et al. (1992) Science 258, 1658-1662]. Here we measure thermal stability profiles of **empty** versus peptide-filled molecules and compare the effects of human versus murine light chains on the overall stability of the Kd heterodimer. The majority of **empty** heterodimers are stable at 37 degrees C regardless of the species of light chain, indicating that our previous report of the unexpectedly high thermal stability was an intrinsic property of the Kd molecule and not due to use of a murine/human chimeric protein. Binding constants are derived for a series of peptides interacting with **empty** Kd heterodimers. The dissociation constants of four known Kd-restricted peptides range from 2.3 x 10(-7) to 3.4 x 10(-8) M. Using a series of 24 analog peptides, the effects of length and peptide composition on binding affinity of one Kd-restricted peptide are explored, and the results are interpreted with reference to the known three-dimensional structures of **class I MHC** protein/peptide complexes.

L4 ANSWER 54 OF 82 MEDLINE
ACCESSION NUMBER: 94246167 MEDLINE
DOCUMENT NUMBER: 94246167 PubMed ID: 8189046
TITLE: Expression of secreted and glycosylphosphatidylinositol-bound Qa-2 molecules is dependent on functional TAP-2 peptide transporter.
AUTHOR: Tabaczewski P; Stroynowski I
CORPORATE SOURCE: Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235.
CONTRACT NUMBER: AI 19624 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1994 Jun 1) 152 (11) 5268-74.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940629
Last Updated on STN: 19940629
Entered Medline: 19940621

AB The assembly of class Ia **MHC** Ags is thought to occur in the endoplasmic reticulum (ER) where H chains, beta 2m, and peptides come together to form trimers. Several types of proteins are implicated in the regulation of class Ia **MHC** assembly, including: 1) TAP1/TAP2 transporters, which translocate peptides derived from naturally processed endogenous proteins from the cytosol into the ER and which are necessary for expression of "peptide-filled" class Ia Ags, and 2) calnexin, a chaperone protein, which was proposed to retain unassembled class Ia chains in the ER. In our study, we examined if the expression of class Ib Qa-2 molecules depends on the TAP1/TAP2 peptide delivery system. The glycosylphosphatidylinositol-linked GPIQa-2 and soluble SQa-2 molecules lack transmembrane regions and consensus calnexin binding sites. Because of these structural features, they were thought to differ from class Ia Ags in cellular trafficking pathways and peptide-binding mechanisms. We find that in TAP2 negative RMA-S cells, the great majority of GPIQa-2 and SQa-2 behave as "**empty**" heterodimers: They cannot maintain stable conformations at 37 degrees C, but their half-lives can be significantly extended by reducing the temperature to 26 degrees C. These results suggest that the Qa-2 binding peptides are delivered to Qa-2 molecules in a manner similar to the class Ia **MHC** Ag system and, therefore, that both GPIQa-2 and SQa-2 may be assembled in the ER. Detection of a small population of heat-resistant Qa-2 molecules in RMA-S is indicative of an alternative, but minor, peptide delivery pathway, or "leakiness" of the RMA-S mutation.

L4 ANSWER 55 OF 82 MEDLINE
ACCESSION NUMBER: 95045915 MEDLINE
DOCUMENT NUMBER: 95045915 PubMed ID: 7525300
TITLE: In vitro priming of cytotoxic T lymphocytes against poorly immunogenic epitopes by engineered antigen-presenting cells.
AUTHOR: Bellone M; Iezzi G; Manfredi A A; Protti M P; Dellabona P; Casorati G; Rugarli C
CORPORATE SOURCE: Istituto Scientifico H. San Raffaele, Milan, Italy.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1994 Nov) 24 (11) 2691-8.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19970203
Entered Medline: 19941221

AB Cytotoxic T lymphocytes (CTL) recognize antigenic peptides presented by major histocompatibility complex **class I** (**MHC**-I) molecules on the surface of target cells. Optimal induction of CD8+ CTL depends on the amount of relevant peptide/**MHC**-I complexes and the presence of co-stimulatory molecules on antigen-presenting cells (APC). The antigen-processing defective mutant cell line RMA-S, when cultured at low temperature, expresses high amounts of **MHC**-I molecules that do not contain endogenously derived peptides. These "

empty" MHC-I molecules can be stabilized by addition of MHC-binding peptides. RMA-S cultured at low temperatures with selected peptides have been used for in vitro CTL induction with conflicting results. RMA-S cells do not express detectable amounts of B7 co-stimulatory molecule. This could explain their unpredictable efficiency as APC. We have evaluated whether RMA-S cells, stably transfected with cDNA encoding for the human B7.1 molecule could provide effective co-stimulation for CD8+ T lymphocytes. RMA-S/B7 cells, loaded with different synthetic peptides, demonstrated a high and sometimes unique efficiency for in vitro primary CTL induction, even when "sub-optimal" antigen peptides were used. Most importantly, RMA-S/B7 cells pulsed with naturally processed peptides extracted from the poorly immunogenic B16 melanoma cells were able to prime CD8+ cells against B16 melanoma. We conclude that the use of RMA-S/B7 cells as APC represents an ideal strategy for in vitro CTL immunization without prior in vivo priming. This system may also help to address the issue of the different contributions of co-stimulation and relative occupancy of MHC-I by single peptide epitopes in CTL priming.

L4 ANSWER 56 OF 82 MEDLINE
ACCESSION NUMBER: 94374420 MEDLINE
DOCUMENT NUMBER: 94374420 PubMed ID: 7522161
TITLE: Major histocompatibility complex class I allele-specific peptide libraries: identification of peptides that mimic an H-Y T cell epitope.
AUTHOR: Gavin M A; Dere B; Grandea A G 3rd; Hogquist K A; Bevan M J
CORPORATE SOURCE: Department of Immunology, University of Washington, Seattle 98195.
CONTRACT NUMBER: AI-19335 (NIAID)
CA-90537 (NCI)
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1994 Sep) 24 (9) 2124-33.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941031
Last Updated on STN: 19960129
Entered Medline: 19941018
AB We describe a novel method for screening large libraries of random peptides for T cell antigens. Two libraries were constructed, containing fixed amino acids representing the major histocompatibility complex (MHC) class I anchor residues for H-2Kb-restricted octamers and H-2Db-restricted nonamers. Peptides from the Kb-restricted library (KbL: SXIXFXXL) and the Db-restricted library (DbL: XXXXNXXXIM) specifically stabilize empty Kb and Db molecules, respectively. The libraries contain peptides that mimic several H-2b-restricted cytotoxic T lymphocyte epitopes, and 21 mimotopes for a Db-restricted H-Y epitope were isolated. A degenerate synthetic peptide of limited complexity containing the identified H-Y sequence motif was found to be similar to the natural H-Y epitope by reverse-phase high performance liquid chromatography analysis. This peptide is also capable of immunizing female mice against male splenocytes. Several applications for MHC -restricted peptide libraries are discussed.

L4 ANSWER 57 OF 82 MEDLINE
ACCESSION NUMBER: 95053706 MEDLINE
DOCUMENT NUMBER: 95053706 PubMed ID: 7525837
TITLE: Analysis of the structure of empty and peptide-loaded major histocompatibility complex molecules at the cell surface.
AUTHOR: Catipovic B; Talluri G; Oh J; Wei T; Su X M; Johansen T E; Edidin M; Schneck J P
CORPORATE SOURCE: Department of Medicine, Johns Hopkins School of Medicine, Baltimore, Maryland 21224.
CONTRACT NUMBER: R37 AI-4584 (NIAID)
RO1 AI-29575 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1994 Nov 1) 180 (5) 1753-61.
Journal code: I2V; 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19960129
Entered Medline: 19941201
AB We compared the conformation of empty and peptide-loaded class I major histocompatibility complex (MHC) molecules at the cell surface. Molecular conformations were analyzed by fluorescence resonance energy transfer (FRET) between fluorescent-labeled Fab fragments bound to the alpha 2 domain of the MHC heavy chain and fluorescent-labeled Fab fragments bound to beta 2-microglobulin. No FRET was found between Fab fragments bound to empty H-2Kb, but FRET was detected when empty H-2Kb molecules were loaded with peptide. The magnitude of FRET depended on the sequence of the peptide used. The results imply that empty H-2Kb molecules are in a relatively extended conformation, and that this conformation becomes more compact when peptide is bound. These changes, which are reflected in peptide-dependent binding of monoclonal antibodies, affect the surfaces of MHC molecules available for contact with T cell receptors and hence may influence T cell-receptor recognition of MHC molecules.

L4 ANSWER 58 OF 82 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 94132615 MEDLINE
DOCUMENT NUMBER: 94132615 PubMed ID: 8301124
TITLE: A monoclonal antibody that recognizes HLA-B27 in the context of peptides.
AUTHOR: Wang J; Yu D T; Fukazawa T; Kellner H; Wen J; Cheng X K; Roth G; Williams K M; Raybourne R B
CORPORATE SOURCE: Department of Medicine, University of California Los Angeles 90024.
CONTRACT NUMBER: CA-16042 (NCI)
PO1 AR40919 (NIAMS)
SOURCE: JOURNAL OF IMMUNOLOGY, (1994 Feb 1) 152 (3) 1197-205.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940318
Last Updated on STN: 19990129
Entered Medline: 19940309

AB The T2 mutant cell line is unable to load peptides into the **MHC class I** Ags inside the cells. These "**empty**" **MHC class I** Ags are not expressed on the cell surface unless the cells are cultured at low temperatures. Expression will occur at 37 degrees C only in the presence of peptides that bind to and stabilize the **class I** Ags. T2 cells transfected with the B*2705 gene were tested with a panel of anti-HLA-B27 mAb. Two of the antibodies, ME1 and KS3, reacted with the "**empty**" HLA-B27 expressed at low culture temperatures. Three antibodies, B27.M1, B27.M2, and Ye-2, were unreactive with these "**empty**" HLA-B27. The cells were then incubated with a panel of HLA-B27-binding peptides. One of the antibodies, Ye-2, became reactive when the cells were incubated with a peptide derived from HIV gp120 and to a less degree with a peptide derived from histone H3.3. Mouse L cells transfected with the B*2705 and the human beta 2m genes also reacted very poorly with B27.M1, B27.M2, and Ye-2. Those two peptides were also able to induce high increase in Ye-2 reactivity. Alternately, increase in Ye-2 reactivity was also observed when the L cells were incubated with IFN-gamma or TNF-alpha. These experiments indicate that the Ye-2 anti-HLA-B27 mAb recognizes HLA-B27 in the context of certain residing peptides either added exogenously or expressed endogenously. The B27.M1 and B27.M2 antibodies might share similar characteristics.

L4 ANSWER 59 OF 82 MEDLINE
ACCESSION NUMBER: 95323666 MEDLINE
DOCUMENT NUMBER: 95323666 PubMed ID: 7600289
TITLE: Protein transfer of preformed **MHC**-peptide complexes sensitizes target cells to T cell cytolysis.
AUTHOR: Huang J H; Getty R R; Chisari F V; Fowler P; Greenspan N S; Tykocinski M L
CORPORATE SOURCE: Institute of Pathology, Case Western Reserve University, Cleveland, Ohio 44106, USA.
CONTRACT NUMBER: P01 DK38181 (NIDDK)
R01 AI20001 (NIAID)
R01 AI31044 (NIAID)
SOURCE: IMMUNITY, (1994 Oct) 1 (7) 607-13.
Journal code: CCF; 9432918. ISSN: 1074-7613.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950822
Last Updated on STN: 19950822
Entered Medline: 19950810

AB Recombinant GPI-anchored HLA-A2.1 (HLA-A2.1-GPI/beta 2m) was used as a protein transfer vehicle to deliver a hepatitis B virus antigenic peptide to the surfaces of cytotoxic T cell targets. **Empty** HLA-A2.1-GPI/beta 2m was first produced in D. melanogaster cotransfectants and immunoaffinity purified. Cell coating with HLA-A2.1-GPI/beta 2m was shown to occur rapidly, and to be protein concentration dependent. Protein-transferred HLA-A2.1-GPI/beta 2m effectively presented a hepatitis B virus peptide to peptide-specific HLA-A2.1-restricted T cell clones in cytotoxicity assays. Protein transfer of functional GPI-modified **class I MHC**-antigenic peptide complexes represents a novel strategy for delivering functional antigenic complexes to cell surfaces that bypasses limitations of gene transfer and permits control of antigenic peptide densities at cell surfaces.

L4 ANSWER 60 OF 82 MEDLINE
ACCESSION NUMBER: 94248687 MEDLINE
DOCUMENT NUMBER: 94248687 PubMed ID: 8191222
TITLE: Interaction of in vitro- and in vivo-generated cytotoxic T cells with SV40 T antigen: analysis with synthetic peptides.
AUTHOR: Alsheikhly A R
CORPORATE SOURCE: Department of Immunology, Scripps Research Institute, La Jolla, CA.
SOURCE: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1994 May) 39 (5) 467-79.
Journal code: UCW; 0323767. ISSN: 0300-9475.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940629
Last Updated on STN: 19970203
Entered Medline: 19940620

AB Virus-specific cytotoxic T cells recognize antigens in the form of peptides (8 or 9 amino acids long) bound to **MHC class-I** molecules. Exposure of unprimed murine splenocytes to synthetic peptides of viral antigens elicits primary CTL in vitro. The fine specificity of such CTL as well as the correlation between binding affinity of peptides to **class-I** molecules and CTL induction was analysed using synthetic peptides corresponding to overlapping and distinct amino-acid residues in SV40 T antigen (Tag) Db-restricted T-cell epitopes I, II-III, and V. The peptides induced cross-reactive CD8+ primary CTL in splenocytes of naive C57 BL/6 mice. This reactivity was seen regardless of the peptides allelic anchor motifs or their abilities to stabilize **empty class-I** molecules. However, none of the primary CTL and CTL lines lysed Tag-expressing cells. In contrast, CTL generated in vivo by immunizing mice with Tag-expressing cells recognized endogenously processed Tag as well as synthetic peptides. The peptides recognized by these CTL depended on the intracellular concentration of Tag antigen in the immunizing cells. The reactivity of these CTL was peptide specific as shown by a functional peptide competition assay. Moreover, three peptides bound to and were recognized in the context of both Kb and Db molecules. These results have revealed a flexible disposition of **MHC class-I** molecules with regard to peptide binding and also reflected lack of correlation between binding affinity to **class-I** molecules and the capacity of peptides to induce primary CTL or to serve as potential targets. The significance of these findings in relation to identifying major T-cell epitopes using allele specific peptide motif and in vitro maintained CTL clones is discussed.

L4 ANSWER 61 OF 82 MEDLINE
ACCESSION NUMBER: 94130956 MEDLINE

DOCUMENT NUMBER: 94130956 PubMed ID: 8299688
TITLE: A quantitative assay to measure the interaction between immunogenic peptides and purified **class I** major histocompatibility complex molecules.
AUTHOR: Olsen A C; Pedersen L O; Hansen A S; Nissen M H; Olsen M; Hansen P R; Holm A; Buus S
CORPORATE SOURCE: Institute for Medical Microbiology and Immunology, Medical Faculty, University of Copenhagen, Denmark.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1994 Feb) 24 (2) 385-92. Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940318
Last Updated on STN: 19940318
Entered Medline: 19940309

AB A direct and sensitive biochemical assay to measure the interaction in solution between peptides and affinity-purified major histocompatibility complex (**MHC**) **class I** molecules has been generated. Specific binding reflecting the known **class I** restriction of cytotoxic T cell responses was obtained. Adding an excess of beta 2-microglobulin (beta 2m) significantly increased the rate of peptide association, but it did not affect the rate of dissociation. Binding was complicated by a rapid and apparently irreversible loss of functional **MHC class I** at 37 degrees C which might limit the life span of **empty MHC class I** thereby preventing the inadvertent exchange of peptides at the target cell surface. All **class I** molecules tested bound peptides of the canonical octa- to nona-meric length. However, one **class I** molecule, Kk, also bound peptides, which were much longer suggesting that the preference of **class I** molecules for short epitopes is not absolute and may be caused by factors other than the peptide-**MHC class I** binding event itself.

L4 ANSWER 62 OF 82 MEDLINE
ACCESSION NUMBER: 94206888 MEDLINE
DOCUMENT NUMBER: 94206888 PubMed ID: 8155603
TITLE: Phosphatidyl inositol-linked forms of a murine **class I MHC** molecule expressed on Chinese hamster ovary cells retain peptide binding capability and alloreactivity.
AUTHOR: Fahnestock M L; Dadgari J M; McMillan M; Bjorkman P J
CORPORATE SOURCE: Howard Hughes Medical Institute, California Institute of Technology, Pasadena 91125.
CONTRACT NUMBER: AI28931 (NIAID)
CA08499 (NCI)
GM36804 (NIGMS)
SOURCE: INTERNATIONAL IMMUNOLOGY, (1994 Feb) 6 (2) 307-14. Journal code: AY5; 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940526
Last Updated on STN: 19970203
Entered Medline: 19940513

AB A gene encoding a phosphatidyl inositol-linked form of the murine **class I MHC** molecule H-2Kd was constructed and the protein expressed in Chinese hamster ovary cells together with murine or human beta 2-microglobulin (beta 2m). The resulting lipid-linked **class I** heterodimers can be efficiently converted into a soluble form by treatment of transfected cells with a phospholipase. Cells expressing Kd heterodimers were characterized with respect to heavy chain levels at the cell surface, peptide binding, and recognition by Kd-specific antibodies and alloreactive cytotoxic T cells. All transfectants bound a 3H-labeled Kd-restricted nonamer peptide, although more peptide bound to cells expressing the Kd/human beta 2m combination, perhaps because of a greater number of **empty** molecules at the cell surface. A dissociation constant of 5 x 10(-8) M derived by Scatchard analysis is within the range expected for interactions of peptides with **class I MHC** molecules. Alloreactive cytotoxic T cells which recognize wild-type Kd on murine cells lysed the hamster cells expressing lipid-linked Kd without regard to the species of the beta 2m light chain. These results indicated that the engineered lipid-linked Kd molecule is expressed at the cell surface, is recognized by antibodies and T cells, and functions to bind peptide.

L4 ANSWER 63 OF 82 MEDLINE
ACCESSION NUMBER: 95317152 MEDLINE
DOCUMENT NUMBER: 95317152 PubMed ID: 7796678
TITLE: Prospects for T cell immunotherapy of tumours by vaccination with immunodominant and subdominant peptides.
AUTHOR: Melief C J; Kast W M
CORPORATE SOURCE: Department of Immunohematology, University Hospital Leiden, The Netherlands.
SOURCE: CIBA FOUNDATION SYMPOSIUM, (1994) 187 97-104; discussion 104-12. Ref: 25
Journal code: D7X; 0356636. ISSN: 0300-5208.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950817
Last Updated on STN: 19970203
Entered Medline: 19950803

AB Immunotherapy of tumours by adoptive transfer of cytotoxic T lymphocytes (CTL) is now feasible in experimental murine systems. These CTL recognize peptide sequences of defined length presented by major histocompatibility complex (**MHC**) **class I** molecules. Effective eradication of large tumour masses requires co-administration of interleukin 2. Tumour escape strategies are numerous but in various instances can be counteracted by defined measures. Initiation of CTL responses against poorly immunogenic virally induced tumours and other tumours requires novel strategies to overcome T cell inertia. We propose a strategy in which CTL are raised against target molecules of choice including differentiation antigens of restricted tissue distribution

(autoantigens) or mutated/overexpressed oncogene products. The steps proposed include: (1) identification of target molecules of choice. (2) Identification in these target molecules of peptides fitting MHC allele-specific peptide motifs involved in peptide binding to MHC molecules. (3) Evaluation of actual binding of such peptides to specific MHC class I molecules. (4) In vitro CTL response induction by such peptides, presented by highly efficient antigen-presenting cells such as antigen processing-defective cells carrying empty MHC class I molecules loaded with a single peptide or dendritic cells. Both types of cells are capable of primary CTL response induction in vitro. (5) Evaluation of proper processing by the demonstration of tumour cell lysis by these CTL. (6) Adoptive transfer of tumour-specific CTL generated in vitro or vaccination with peptides. These various steps have now been taken for several viruses, virally induced tumours and other types of tumours and the first indications that this strategy is useful have been obtained.

L4 ANSWER 64 OF 82 MEDLINE
ACCESSION NUMBER: 94217811 MEDLINE
DOCUMENT NUMBER: 94217811 PubMed ID: 8164742
TITLE: CTL induction by a tumour-associated antigen octapeptide derived from a murine lung carcinoma.
COMMENT: Comment in: Nature. 1994 Jun 2;369(6479):357
Erratum in: Nature 1997 Dec 11;390(6660):643
AUTHOR: Mandelboim O; Berke G; Fridkin M; Feldman M; Eisenstein M; Eisenbach L
CORPORATE SOURCE: Department of Cell Biology, Weizmann Institute of Science, Rehovot, Israel.
SOURCE: NATURE, (1994 May 5) 369 (6475) 67-71.
Journal code: NSC; 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940606
Last Updated on STN: 20000303
Entered Medline: 19940524

AB Many mouse and human tumours express major histocompatibility complex (MHC) class I-associated antigens that constitute targets for syngeneic cytotoxic T lymphocytes (CTL). Genes encoding such antigens were isolated from a mouse mastocytoma and from human melanomas by genetic methods. Isolation and characterization of MHC class I-associated peptides has enabled specific anchor residues to be identified that are typical of peptides that bind to distinct class I molecules. Moreover, CTL specific to particular MHC-peptide combinations have been used to identify naturally occurring antigenic peptides in cell extracts and enabled them to be sequenced directly. Most known MHC ligands are of viral origin or are self peptides derived from normal proteins. Here we use total acid extraction and repeated fractionation to isolate and sequence Lewis lung carcinoma (3LL)-specific peptide(s), which shows sequence homology to the connexin 37 protein. Synthetic octamers based on these sequences bind to 'empty' H-2Kb molecules on RMA-S cells, sensitize RMA-S cells to lysis by specific anti-3LL CTL, and induce anti-tumour CTL. The tumour-associated peptide originates from mutated connexin 37 expressed in 3LL.

L4 ANSWER 65 OF 82 MEDLINE
ACCESSION NUMBER: 93389135 MEDLINE
DOCUMENT NUMBER: 93389135 PubMed ID: 7690793
TITLE: Dynamics of peptide binding to purified antibody-bound H-2Db and H-2Db beta 2m complexes.
AUTHOR: Burshtyn D N; Barber B H
CORPORATE SOURCE: Department of Immunology, University of Toronto, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Sep 15) 151 (6) 3082-93.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931105
Last Updated on STN: 19970203
Entered Medline: 19931020

AB Although it is clear that each component of the class I MHC trimolecular complex (heavy chain, beta 2m, and antigenic peptide) contributes to its formation and stability, the specific interaction governing assembly and disassembly remain to be clarified. In an effort to address these issues using purified H-2Db molecules, we used a solid-phase binding assay recently developed in our laboratory to quantify kinetic parameters for class I assembly and disassembly. It was found that the influenza NP peptide Y367-374 associated with preformed empty complexes of 28-14-8S- (i.e., anti-alpha 3) bound Db beta 2m dimers much more quickly (t 1/2 < 0.2 h at 22 degrees C) than it did when coincubated with an anti-alpha 3 bound Db and human beta 2m (t1/2 3.5 h at 22 degrees C). The previously reported potential for the NP peptide Y367-374 to interact directly with free Db heavy chains and configure the conventionally beta 2m-dependent B22 epitope in the absence of beta 2m, was confirmed using our assay system. However, the rate of B22 epitope formation induced in the Db heavy chain by NP Y367-374 was considerably slower (t1/2 13 h, at 22 degrees C) and much less efficient on a molar basis than that resulting from the addition of beta2m (t1/2, 0.75 h, at 22 degrees C). In contrast, the Db heavy chain with NP-Y367-374 was more resistant to thermal disassembly (as measured by loss of the B22 epitope, t1/2 2h, 37 degrees C) than the Db beta 2m empty dimer (t1/2 0.2 h). Finally, stability of the preformed trimolecular complex of heavy chain, beta 2m, and peptide was found to diminish in accordance with deviation of the peptide from the optimal length and with increasing temperature from 4 to 37 degrees C.

L4 ANSWER 66 OF 82 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 93389134 MEDLINE
DOCUMENT NUMBER: 93389134 PubMed ID: 8397250
TITLE: High occupancy binding of antigenic peptides to purified, immunoadsorbed H-2Db beta 2m molecules.
AUTHOR: Burshtyn D N; Barber B H
CORPORATE SOURCE: Department of Immunology, University of Toronto, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Sep 15) 151 (6) 3070-81.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931105
Last Updated on STN: 19970203
Entered Medline: 19931020

AB In an effort to examine the peptide binding properties of purified **class I MHC** molecules, we have developed a solid phase, radiolabeled peptide binding assay based on the use of H-2Db molecules bound to agarose **beads** via heavy chain-specific mAb. Using purified Db beta 2m, recovered from RMA-S cells and bound to immunoadsorbent **beads** through either alpha 1 or alpha 3 region specific antibodies, complete occupancy of these molecules could be achieved with 125I-Y366-374 influenza nucleoprotein peptide (Kd 10(-7) M). Approximately 12% of the Db beta 2m dimers recovered from RMA cells could be occupied by this influenza nucleoprotein peptide under the same conditions. When free Db heavy chains were isolated from beta 2m negative R1E.Db cells by **bead**-bound alpha 3-region specific antibody (28-14-8S) and were incubated with human beta 2m, high affinity (Kd 10(-8) M) binding sites were created for the 125I-Y367-374 influenza nucleoprotein peptide. In addition to demonstrating that a significant fraction of the heavy chains present in R1E.Db cells are in a beta 2m-reactive form, the R1E.Db cells provide an alternate approach to that of RMA-S derived Db beta 2m **empties** for the creation of homogeneous complexes of Db, beta 2m, and antigenic peptide. We anticipate that these **bead**-bound **empty** and defined peptide-**class I** complexes may be useful in the further study of **class I MHC** target structure formation and recognition.

L4 ANSWER 67 OF 82 MEDLINE
ACCESSION NUMBER: 93345566 MEDLINE
DOCUMENT NUMBER: 93345566 PubMed ID: 7688306
TITLE: Reduced expression of major histocompatibility complex **class** I free heavy chains and enhanced sensitivity to natural killer cells after incubation of human lymphoid lines with beta 2-microglobulin.
AUTHOR: Carbone E; Stuber G; Andree S; Franksson L; Klein E; Beretta A; Siccardi A G; Karre K
CORPORATE SOURCE: Department of Tumor Biology, Karolinska Institute, Stockholm, Sweden.
CONTRACT NUMBER: 1 RO1 CA-44882-01 (NCI)
5 RO1 CA-25250-06 (NCI)
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 Aug) 23 (8) 1752-6.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19930924
Last Updated on STN: 19960129
Entered Medline: 19930903

AB Enhancement of major histocompatibility complex (**MHC**) **class I** expression leads to protection from recognition by natural killer (NK) cells in several systems. **MHC class I** gene products can be expressed in different forms at the cell surface--for example as "**empty**" beta 2-microglobulin (beta 2m)-associated heterodimers or free heavy chains. To study the role of different **class I** heavy chain forms in NK target interactions, we have used lymphoblastoid target cell lines preincubated with beta 2m. This was found to shift the equilibrium between beta 2m-associated and non-associated--heavy chains in favor of the former. In parallel, there was a significant increase in NK sensitivity. The recognition of **MHC class I**-deficient cell lines was not affected by beta 2m, arguing against a general nonspecific effect of beta 2m on NK sensitivity. Our data indicate that protection against NK recognition correlates with target cell expression of free heavy chains (i.e. devoid of beta 2m) rather than with expression of complexes.

L4 ANSWER 68 OF 82 MEDLINE
ACCESSION NUMBER: 93238869 MEDLINE
DOCUMENT NUMBER: 93238869 PubMed ID: 8477806
TITLE: Real-time measurement of antigenic peptide binding to **empty** and preloaded single-chain major histocompatibility complex **class** I molecules.
AUTHOR: Ojcius D M; Godeau F; Abastado J P; Casanova J L; Kourilsky P
CORPORATE SOURCE: Institut Pasteur, INSERM U.277, Paris, France.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 May) 23 (5) 1118-24.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930611
Last Updated on STN: 19970203
Entered Medline: 19930525

AB Cytotoxic T lymphocytes (CTL) recognize peptides in association with major histocompatibility complex (**MHC**) **class I** proteins, but how peptides bind to **class I** is not well understood. We used a fluorescence technique to measure antigenic peptide binding to a soluble, single-chain Kd (SC-Kd) molecule in which the Kd heavy chain was connected by a 15-residue link to beta 2-microglobulin. Peptides were covalently labeled at their N terminus with dansyl, and binding of dansylated Kd-restricted peptides to SC-Kd resulted in significant fluorescence enhancement, which could be inhibited by unmodified Kd-restricted peptides. Real-time binding of a dansylated peptide could be followed by monitoring the fluorescence at 530 nm. The dansylated Plasmodium berghei circumsporozoite (PbCS) 263-260 peptide bound to "**empty**" SC-Kd with an association rate constant of 1140 M-1s-1, and the subsequent spontaneous dissociation of the SC-Kd-peptide complex was slow. The dissociation increased dramatically after addition of excess unlabeled PbCS 253-260 peptide, but with a slower association constant for unlabeled peptide, 77 M-1s-1. Thus, the Kd-peptide complex on the surface of antigen-presenting cells should be stable, but high concentrations of peptides in the endoplasmic reticulum (ER) lumen would allow for peptide exchange on Kd before export to the surface. The apparent activation energy for PbCS 253-260 peptide binding to SC-Kd was 6.78 +/- 0.64 kcal/mole, similar to values previously reported for

antigen-antibody interactions.

L4 ANSWER 69 OF 82 MEDLINE
ACCESSION NUMBER: 93088081 MEDLINE
DOCUMENT NUMBER: 93088081 PubMed ID: 1360705
TITLE: Thermal stability comparison of purified **empty** and peptide-filled forms of a **class I** **MHC** molecule.
AUTHOR: Fahnestock M L; Tamir I; Narhi L; Bjorkman P J
CORPORATE SOURCE: Division of Biology, California Institute of Technology, Pasadena 91125.
CONTRACT NUMBER: AI28931 (NIAID)
SOURCE: SCIENCE, (1992 Dec 4) 258 (5088) 1658-62.
Journal code: UJ7; 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 19930129
Last Updated on STN: 19950206
Entered Medline: 19930107

AB A secreted form of a **class I** major histocompatibility complex (**MHC**) molecule was denatured and renatured in vitro in the absence of peptide. The resulting **empty class** **I** heterodimer was immunologically reactive and structurally similar to a heterodimer renatured in the presence of an appropriate restricted peptide. Thermal stability profiles indicated that the two forms of heterodimer differed in their resistance to denaturation by heat but that a significant portion of the **empty class** **I** heterodimers had a native conformation at physiological temperatures. Free energies calculated from these data gave a direct measure of the stabilization of the **class I** **MHC** molecule that resulted from peptide binding.

L4 ANSWER 70 OF 82 MEDLINE
ACCESSION NUMBER: 93094765 MEDLINE
DOCUMENT NUMBER: 93094765 PubMed ID: 1281212
TITLE: Major histocompatibility complex conformational epitopes are peptide specific.
AUTHOR: Catipovic B; Dal Porto J; Mage M; Johansen T E; Schneck J P
CORPORATE SOURCE: Department of Medicine, Johns Hopkins University School of Medicine, Johns Hopkins University, Baltimore, Maryland 21224.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1992 Dec 1) 176 (6) 1611-8.
Journal code: I2V; 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 19930129
Last Updated on STN: 19980206
Entered Medline: 19930108

AB Serologically distinct forms of H-2Kb are stabilized by loading cells expressing "**empty**" **class** **I** major histocompatibility complex (**MHC**) molecules with different H-2Kb binding peptides. The H-2Kb epitope recognized by monoclonal antibody (mAb) 28.8.6 was stabilized by ovalbumin (OVA) (257-264) and murine cytomegalovirus (MCMV) pp89 (168-176) peptides, but not by vesicular stomatic virus nucleoprotein (VSV NP) (52-59) and influenza NP (Y345-360) peptides. The H-2Kb epitope recognized by mAb 34.4.20 was stabilized by VSV NP (52-59) peptide but not by OVA (257-264), MCMV pp89 (168-176), or influenza NP (Y345-360) peptides. Immunoprecipitation of H-2Kb molecules from normal cells showed that 28.8.6 and 34.4.20 epitopes were only present on a subset of all conformationally reactive H-2Kb molecules. Using alanine-substituted derivatives of the VSV peptide, the 28.8.6 epitope was completely stabilized by substitution of the first residue and partially stabilized by substitution of the third or the fifth residues in the peptides. These results indicate that distinct conformational **MHC** epitopes are dependent on the specific peptide that occupies the antigenic peptide binding groove on individual **MHC** molecules. The changes in **MHC** epitopes observed may also be important in understanding the diversity of T cell receptors used in an immune response and the influence of peptides on development of the T cell repertoire.

L4 ANSWER 71 OF 82 MEDLINE
ACCESSION NUMBER: 92289822 MEDLINE
DOCUMENT NUMBER: 92289822 PubMed ID: 1376267
TITLE: Preferred size of peptides that bind to H-2 Kb is sequence dependent.
AUTHOR: Deres K; Schumacher T N; Wiesmuller K H; Stevanovic S; Greiner G; Jung G; Ploegh H L
CORPORATE SOURCE: Institut fur Organische Chemie, Universitat Tubingen.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1992 Jun) 22 (6) 1603-8.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920724
Last Updated on STN: 19970203
Entered Medline: 19920714

AB The identification of naturally processed viral peptides reveals that major histocompatibility complex (**MHC**) **class** **I** epitopes are composed of nine or eight amino acid residues. Peptides eluted from H-2 Kb **MHC** **class** **I** molecules have been suggested, as a class, to be eight amino acid residues long. To assay for peptide-**class** **I** interactions, a stabilization assay described for surface labeled "**empty**" **class** **I** molecules was employed, but on biosynthetically labeled **class** **I** molecules. The Sendai virus nucleoprotein-derived octapeptide APGNYPAL does not bind and stabilize Kb molecules, whereas other octameric Kb-restricted peptides and the nonameric peptide FAPGNYPAL interact stably. We attribute the failure of Sendai octamer binding to the presence of proline in position two: replacement of proline renders the resulting octamers as efficient as FAPGNYPAL for binding and stabilization of H-2 Kb. Substitution of glycine in position three of APGNYPAL slightly improves its Kb stabilizing capacity. Iodination of the tyrosine residue significantly alters the

binding properties of the nonamer peptide. We conclude that the length of epitopes as selected by the **class I** Kb molecule is influenced by their sequence and suggest that proper positioning of the NH2 terminus of peptides is essential for **class I** stabilizing properties. The ability to stabilize newly synthesized " **empty" class I** molecules with peptide argues against an involvement of beta 2 microglobulin exchange in the experiments described here.

L4 ANSWER 72 OF 82 MEDLINE
ACCESSION NUMBER: 93041480 MEDLINE
DOCUMENT NUMBER: 93041480 PubMed ID: 1384686
TITLE: Peptide-conjugated hapten groups are the major antigenic determinants for trinitrophenyl-specific cytotoxic T cells.
AUTHOR: von Bonin A; Ortmann B; Martin S; Weltzien H U
CORPORATE SOURCE: Max-Planck-Institut fur Immunbiologie, Freiburg, Germany.
SOURCE: INTERNATIONAL IMMUNOLOGY, (1992 Aug) 4 (8) 869-74.
Journal code: AY5; 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19960129
Entered Medline: 19921221

AB Several trinitrophenyl (TNP)-specific mouse cytotoxic T cell (CTL) clones recognize TNP-conjugated peptides in association with **class I MHC** molecules ('hapten-peptide determinants'). However, cell modification with trinitrobenzene sulfonic acid (TNBS) also leads to the formation of TNP determinants covalently attached to **MHC** molecules ('altered self'). To determine the importance of 'peptide' versus 'altered self' determinants, we used the mutant cell line RMA-S which expresses peptide-free ('**empty**') Kb and Db molecules at 26 degrees C. Additionally, we stabilized Kb molecules on RMA-S cells at 37 degrees C using the Kb binding heptapeptide N53-59 derived from the vesicular stomatitis virus nucleoprotein. Lacking lysine, this peptide remains unmodified by TNBS and, therefore, only allows the formation of 'altered self' TNP determinants on occupied Kb molecules. RMA-S targets, pretreated or untreated with N53-59, upon TNBS modification were only lysed poorly or not at all by four different TNP-specific CTL. In contrast, all of these clones efficiently lysed TNBS-treated, unmutated RMA cells, and three of them strongly reacted with RMA or RMA-S cells in the presence of tryptic TNP-BSA peptides. Moreover, the clone unreactive for TNP-BSA peptides also recognized TNP self-peptides extracted from TNBS-treated syngeneic spleen cells. Taken together, these data clearly show that TNP residues linked to **MHC** via associated peptides but not by covalent bondage represent the dominant antigenic epitopes for **class I MHC**-restricted, hapten-specific T cells.

L4 ANSWER 73 OF 82 MEDLINE
ACCESSION NUMBER: 92212461 MEDLINE
DOCUMENT NUMBER: 92212461 PubMed ID: 1557127
TITLE: HLA-A2 molecules in an antigen-processing mutant cell contain signal sequence-derived peptides.
COMMENT: Comment in: Nature. 1992 Apr 2;356(6368):386-7
Comment in: Nature. 1992 Jul 16;358(6383):198
AUTHOR: Wei M L; Cresswell P
CORPORATE SOURCE: Department of Microbiology and Immunology, Duke University Medical Center, Durham, North Carolina 27710.
SOURCE: NATURE, (1992 Apr 2) 356 (6368) 443-6.
Journal code: NSC; 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920515
Last Updated on STN: 19920515
Entered Medline: 19920506

AB The mutant human cell line T2 is defective in antigen presentation in the context of **class I** major histocompatibility complex (**MHC**) molecules, and also in that transfected T2 cells show poor surface expression of exogenous human **class I** (HLA) alleles. Both defects are thought to lie in the transport of antigenic peptides derived from cytosolic proteins into the endoplasmic reticulum (ER), as peptide-deficient **class I** molecules might be expected to be either unstable or retained in the ER. The products of several mouse **class I** (H-2) genes, and the endogenous gene HLA-A2 do, however, reach the surface of T2 cells at reasonable levels although they are non-functional. We report here that, as expected, poorly surface-expressed HLA molecules do not significantly bind endogenous peptides. Surprisingly, H-2 molecules expressed in T2 also lack associated peptides, arguing that '**empty**' complexes of mouse **class I** glycoproteins with human beta 2-microglobulin are neither retained in the ER nor unstable. HLA-A2 molecules, however, do bind high levels of a limited set of endogenous peptides. We have sequenced three of these peptides and find that two, a 9-mer and an 11-mer, are derived from a putative signal sequence (of IP-30, an interferon-gamma-inducible protein), whereas a third, a 13-mer, is of unknown origin. The unusual length of two of the peptides argues that the 9-mers normally associated with HLA-A2 molecules may be generated before their transport from the cytosol rather than in a pre-Golgi compartment. To our knowledge, this is the first report of the isolation of a fragment of a eukaryotic signal peptide generated in vivo.

L4 ANSWER 74 OF 82 MEDLINE
ACCESSION NUMBER: 93032148 MEDLINE
DOCUMENT NUMBER: 93032148 PubMed ID: 1412716
TITLE: The role of beta-2 microglobulin in temperature-sensitive and interferon-gamma-induced exocytosis of HLA **class** I molecules.
AUTHOR: Tatake R J; Ferrone S; Zeff R A
CORPORATE SOURCE: Department of Pathology, University of Connecticut Health Center, Farmington 06030.
CONTRACT NUMBER: CA 39559 (NCI)
SOURCE: TRANSPLANTATION, (1992 Sep) 54 (3) 395-403.
Journal code: WEJ; 0132144. ISSN: 0041-1337.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921029

AB The passage of **MHC class I** heavy chains through the exocytic pathway is promoted by association with beta 2 microglobulin (beta 2m). In order to analyze the structural basis of this phenomenon, processing and cell surface expression of HLA **class I** molecules have been investigated in the beta 2m null human melanoma cell line FO-1 transfected with either the human or mouse beta 2m genes. These natural structural variants of beta 2m display 30% amino acid sequence divergence. In comparison with a human beta 2m transfectant of the FO-1 cell line (designated FO-1H), FO-1 cells transfected with the mouse beta 2m gene (FO-1C) express HLA **class I** molecules that are processed with grossly altered kinetics and are present on the cell surface at reduced levels. The suboptimal expression of HLA **class I** heavy chains encoded by FO-1C cells reflects a defect in heavy chain stability since cell surface expression of HLA **class I** antigens was increased following incubation at 30 degrees C. The increased cell surface expression paralleled accelerated processing of HLA **class I** heavy chains by FO-1C cells. In contrast, no induction in either cell surface expression or processing of HLA **class I** heavy chains was observed for the beta 2m-negative FO-1 parent cell line, which remained HLA **class I** antigen null when cultured at 30 degrees C, or the FO-1H human beta 2m transfectant, which expressed equivalent levels of HLA **class I** antigens on the cell surface at 37 degrees C and 30 degrees C. Further up-regulation of the temperature-sensitive induction of HLA **class I** antigen expression was accomplished by treatment of the FO-1C transfectant with interferon-gamma; this latter effect appears to be active at a posttranscriptional step for FO-1 cells since IFN-gamma was not as potent a transcriptional activator at 30 degrees C as it was at 37 degrees C. These results indicate that HLA **class I** heavy chains expressed by FO-1C cells are subject to temperature-sensitive and cytokine-inducible stabilization that increases their affinity for the structural variant of beta 2m and promotes exocytosis of the HLA **class I** heterodimer to the cell surface. Furthermore, beta 2m non-conformed **MHC class I** heavy chains undergo stabilization that is not associated with enhanced cell surface expression, indicating that the exocytosis of putative "**empty**" HLA **class I** antigens is a process dependent upon association with beta 2m.

L4 ANSWER 75 OF 82 MEDLINE
ACCESSION NUMBER: 93046232 MEDLINE
DOCUMENT NUMBER: 93046232 PubMed ID: 1423326
TITLE: Lessons from T cell responses to virus induced tumours for cancer eradication in general.
AUTHOR: Melief C J; Kast W M
CORPORATE SOURCE: Department of Immunohematology and Blood Bank, University Hospital, Leiden, Netherlands.
SOURCE: CANCER SURVEYS, (1992) 13 81-99. Ref: 103
Journal code: CNG; 8218015. ISSN: 0261-2429.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921201

AB Immunotherapy of virus induced tumours by adoptive transfer of virus specific cytotoxic T cells (CTL) is now feasible in experimental murine systems. These CTL recognize viral peptide sequences of defined length presented in the groove of **MHC class I** molecules. Effective eradication of large tumour masses requires coadministration of IL-2. In essence, T cell immunity against virus induced tumours does not differ from anti-viral T cell immunity in general. Tumour escape strategies are numerous but, in various instances, can be counteracted by defined measures. Initiation of CTL responses against poorly immunogenic non-virus induced tumours (the majority of human cancer) requires novel strategies to overcome T cell inertia. Rather than waiting to see whether tumour specific CTL (against unknown antigens) can be cultured from TIL, we propose an alternative strategy in which CTL are raised against target molecules of choice, including differentiation antigens of restricted tissue distribution (autoantigens) or mutated/overexpressed oncogene products. The various steps proposed include: (a) identification of target molecules of choice; (b) identification in these target molecules of **MHC** allele specific peptide motifs involved in peptide binding to **MHC** molecules; (c) evaluation of actual binding of such peptides to specific **MHC class I** molecules; (d) in vitro CTL response induction by such peptides, presented either by highly efficient antigen presenting cells (such as processing defective cells, which carry **empty MHC class I** molecules) loaded with a single peptide or by dendritic cells, both cell types being capable of primary CTL response induction in vitro and (e) adoptive transfer of tumour specific CTL generated in vivo or, more conveniently, vaccination with immunodominant peptides. The latter possibility seems to be feasible because peptide vaccination with a single immunodominant viral peptide can install CTL memory and confer protection against lethal virus infection.

L4 ANSWER 76 OF 82 MEDLINE
ACCESSION NUMBER: 92083921 MEDLINE
DOCUMENT NUMBER: 92083921 PubMed ID: 1660811
TITLE: Peptide loading of **empty** major histocompatibility complex molecules on RMA-S cells allows the induction of primary cytotoxic T lymphocyte responses.
AUTHOR: De Bruijn M L; Schumacher T N; Nieland J D; Ploegh H L; Kast W M; Melief C J
CORPORATE SOURCE: Division of Immunology, The Netherlands Cancer Institute, Amsterdam.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Dec) 21 (12) 2963-70.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199201
ENTRY DATE: Entered STN: 19920209
Last Updated on STN: 19970203

Entered Medline: 19920123

AB The antigen processing-defective mutant cell line RMA-S expresses at the cell surface major histocompatibility complex (**MHC**) **class I** molecules devoid of peptide that can be efficiently loaded with exogenous immunogenic peptides. We now report that viral peptide-loaded RMA-S cells, unlike parental RMA cells, can induce primary cytotoxic T lymphocyte (CTL) responses in vitro, in a T helper cell-independent fashion. This was shown for an H-2Kb-binding peptide of Sendai virus nucleoprotein and an H-2Db-binding peptide of adenovirus type 5 E1A protein with responding spleen cells of C57BL/6 mice, the strain of origin of RMA and RMA-S cells. Primary Sendai peptide-induced CTL lyse both peptide-loaded and virus-infected cells. Pre-culture of RMA-S cells at low temperature (22 degrees - 26 degrees C), which increases the amount of **empty MHC class I** molecules at the cell surface, decreases the peptide concentrations required for the induction of primary CTL responses. Primary peptide-specific CTL responses induced by peptide-loaded RMA-S cells are CD4+ cell- and **MHC class II+** cell-independent. CTL response induction is blocked by the presence of anti-CD8 monoclonal antibody during culture. Direct peptide binding studies confirm the efficient loading of **empty MHC** molecules on RMA-S cells with peptide and show 2.5-fold more peptide bound per RMA-S cell compared to RMA cells. An additional factor explaining the difference in primary response induction between RMA and RMA-S cells is related to the CD8 dependence of these responses. **MHC class I** molecules occupied with irrelevant peptides (a majority present on RMA, largely absent on RMA-S) may interfere in the interaction of the CD8 molecule with relevant **MHC** /peptide complexes. The results delineate a novel strategy of peptide based in vitro immunization to elicit CD8+ cytotoxic T cell responses.

L4 ANSWER 77 OF 82 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 91364807 MEDLINE
DOCUMENT NUMBER: 91364807 PubMed ID: 1889467
TITLE: Exogenous beta 2-microglobulin is required for antigenic peptide binding to isolated **class I** major histocompatibility complex molecules.
AUTHOR: Kane K P; Sherman L A; Mescher M F
CORPORATE SOURCE: Division of Membrane Biology, Scripps Clinic and Research Foundation, La Jolla, CA 92037.
CONTRACT NUMBER: AI 24526 (NIAID)
CA 25803 (NCI)
CA 52856 (NCI)
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Sep) 21 (9) 2289-92.
Journal code: EN5; 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911103
Last Updated on STN: 19911103
Entered Medline: 19911011

AB Binding of antigenic peptides to purified **class I** major histocompatibility complex (**MHC**) molecules, as measured by antigen-specific cytolytic T lymphocyte (CTL) degranulation, was found to occur in the presence of serum but not in its absence. The role of soluble beta 2-microglobulin (beta 2m), a normal component of serum, in **class I**-peptide complex formation was therefore examined. Sera depleted of beta 2m did not **support** effective peptide binding to **class I**, but binding was restored in the presence of low concentrations of purified human beta 2m. Sequential incubation of immobilized **class I** with human beta 2m first, followed by peptide, resulted in antigenic complex formation, while reversing the order of pulsing could not. Similar results were obtained in experiments examining H-2Db, Kb and Kd with appropriate peptides and CTL. These results demonstrate that mature **class I** proteins are not able to directly bind peptide, but that interaction with exogenous beta 2m results in a structure that will subsequently bind peptide. Binding of exogenous beta 2m appears to result in "**empty**" **class I** molecules, possibly by exchange for endogenous beta 2m, with a concomitant loss of endogenous peptide.

L4 ANSWER 78 OF 82 MEDLINE
ACCESSION NUMBER: 91218848 MEDLINE
DOCUMENT NUMBER: 91218848 PubMed ID: 1708852
TITLE: Peptide selection by **MHC class I** molecules.
AUTHOR: Schumacher T N; De Bruijn M L; Vernie L N; Kast W M; Melief C J; Neefjes J J; Ploegh H L
CORPORATE SOURCE: Department of Cellular Biochemistry, The Netherlands Cancer Institute, Amsterdam.
SOURCE: NATURE, (1991 Apr 25) 350 (6320) 703-6.
Journal code: NSC; 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910623
Last Updated on STN: 19970203
Entered Medline: 19910531

AB Synthetic peptides have been used to sensitize target cells and thereby screen for epitopes recognized by T cells. Most epitopes of cytotoxic T lymphocytes can be mimicked by synthetic peptides of 12-15 amino acids. Although in specific cases, truncations of peptides improves sensitization of target cells, no optimum length for binding to major histocompatibility complex (**MHC**) **class I** molecules has been defined. We have now analysed synthetic peptide captured by **empty MHC class I** molecules of the mutant cell line RMA-S. We found that **class I** molecules preferentially bound short peptides (nine amino acids) and selectively bound these peptides even when they were a minor component in a mixture of longer peptides. These results may help to explain the difference in size restriction of T-cell epitopes between experiments with synthetic peptides and those with naturally processed peptides.

L4 ANSWER 79 OF 82 MEDLINE
ACCESSION NUMBER: 91293922 MEDLINE
DOCUMENT NUMBER: 91293922 PubMed ID: 2066186
TITLE: Fine peptide specificity of cytotoxic T lymphocytes directed against adenovirus-induced tumours and peptide-**MHC** binding.

AUTHOR: Kast W M; Melief C J
CORPORATE SOURCE: Department of Immunohaematology, Academic Hospital, Leiden, The Netherlands.
SOURCE: INTERNATIONAL JOURNAL OF CANCER. SUPPLEMENT, (1991) 6 90-4. Journal code: GRM; 8710267. ISSN: 0898-6924.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910901
Last Updated on STN: 19910901
Entered Medline: 19910809

AB A peptide encoded by the adenovirus type 5 early region I (Ad5 EI) is the target structure for H-2Db-restricted cytotoxic T lymphocytes (CTL) that are capable of tumour eradication in vivo. With the use of a set of peptides in which each individual amino acid (aa) was deleted out of the sequence, we analyzed to what extent these deletion mutant peptides were still recognized by an Ad5-specific CTL clone and which deletion mutant peptides still bound to major histocompatibility-complex (MHC) class-I molecules. Binding was analyzed with RMA-S cells that express largely empty and unstable MHC-class-I molecules which are stabilized by peptide binding. We show here that flanking an 8 mer aa sequence, originally described by us as the minimal epitope recognized by CTL, 2 additional aa are important for MHC binding. This leads to the conclusion that this 10-mer peptide is optimal for MHC binding and T-cell recognition. Areas of the peptide primarily involved in binding to MHC or in T-cell recognition are delineated.

L4 ANSWER 80 OF 82 MEDLINE
ACCESSION NUMBER: 91087923 MEDLINE
DOCUMENT NUMBER: 91087923 PubMed ID: 1985269
TITLE: Excess beta 2 microglobulin promoting functional peptide association with purified soluble class I MHC molecules.
AUTHOR: Kozlowski S; Takeshita T; Boehncke W H; Takahashi H; Boyd L F; Germain R N; Berzofsky J A; Margulies D H
CORPORATE SOURCE: Molecular Biology Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: NATURE, (1991 Jan 3) 349 (6304) 74-7. Journal code: NSC; 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910322
Last Updated on STN: 19970203
Entered Medline: 19910207

AB T lymphocytes expressing alpha beta receptors recognize antigenic peptide fragments bound to major histocompatibility complex class I or class II molecules present on the surface membranes of other cells. Peptide fragments are present in the two available HLA crystal structures and recent data indicate that peptide is required for the stable folding of the class I heavy chain and maintenance of its association with the class I light chain, beta 2-microglobulin (beta 2m), at physiological temperature. To explain how the exogenous peptide used to create targets for cytotoxic cells bearing CD8 antigen could associate with apparently peptide-filled extracellular class I molecules, we hypothesized that stable binding of exogenous peptide to mature class I molecules reflects either the replacement of previously bound peptide during the well documented beta 2m exchange process or the loading of 'empty' class I heavy chains dependent on the availability of excess beta 2m. In either case, free beta 2m should enhance peptide/class I binding. Using either isolated soluble class I molecules or living cells, we show here that free purified beta 2m markedly augments the generation of antigenic complexes capable of T-cell stimulation.

L4 ANSWER 81 OF 82 MEDLINE
ACCESSION NUMBER: 90335965 MEDLINE
DOCUMENT NUMBER: 90335965 PubMed ID: 2199065
TITLE: Direct binding of peptide to empty MHC class I molecules on intact cells and in vitro.
AUTHOR: Schumacher T N; Heemels M T; Neefjes J J; Kast W M; Melief C J; Ploegh H L
CORPORATE SOURCE: The Netherlands Cancer Institute, Amsterdam.
SOURCE: CELL, (1990 Aug 10) 62 (3) 563-7. Journal code: CQ4; 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901012
Last Updated on STN: 19901012
Entered Medline: 19900913

AB MHC class I molecules devoid of peptide are expressed on the cell surface of the mouse mutant lymphoma cell line RMA-S upon culture at reduced temperature. Empty class I molecules are thermolabile at the cell surface and in detergent lysates, but can be stabilized by the addition of presentable peptide; peptide binding appears to be a rapid process. Furthermore, class I molecules on the surface of RMA-S (H-2b haplotype) cells cultured at 26 degrees C can efficiently and specifically bind iodinated peptide presented by H-2Kb. Binding of iodinated peptide is also observed at a lower level for nonmutant cells (RMA) cultured at 26 degrees C. These experiments underscore the role for peptide in maintenance of the structure of class I molecules and, more importantly, provide two assay systems to study the interactions of peptides with MHC class I molecules independent of the availability of T cells that recognize a particular peptide-MHC class I complex.

L4 ANSWER 82 OF 82 MEDLINE
ACCESSION NUMBER: 90332008 MEDLINE
DOCUMENT NUMBER: 90332008 PubMed ID: 2198471
TITLE: Empty MHC class I molecules come out in the cold.

AUTHOR: Ljunggren H G; Stam N J; Ohlen C; Neefjes J J; Hoglund P; Heemels M T; Bastin J; Schumacher T N; Townsend A; Karre K; +
CORPORATE SOURCE: Department of Tumor Biology, Karolinska Institute, Stockholm, Sweden.
SOURCE: NATURE, (1990 Aug 2) 346 (6283) 476-80. Journal code: NSC; 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901012
Last Updated on STN: 19970203
Entered Medline: 19900906

AB Major histocompatibility complex (**MHC**) **class I** molecules present antigen by transporting peptides from intracellularly degraded proteins to the cell surface for scrutiny by cytotoxic T cells. Recent work suggests that peptide binding may be required for efficient assembly and intracellular transport of **MHC class I** molecules, but it is not clear whether **class I** molecules can ever assemble in the absence of peptide. We report here that culture of the murine lymphoma mutant cell line RMA-S at reduced temperature (19-33 degrees C) promotes assembly, and results in a high level of cell surface expression of H-2/beta 2-microglobulin complexes that do not present endogenous antigens, and are labile at 37 degrees C. They can be stabilized at 37 degrees C by exposure to specific peptides known to interact with H-2Kb or Db. Our findings suggest that, in the absence of peptides, **class I** molecules can assemble but are unstable at body temperature. The induction of such molecules at reduced temperature opens new ways to analyse the nature of **MHC class I** peptide interactions at the cell surface.

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 12:53:02 ON 16 APR 2002
L1 41486 S (MHC AND (CLASS (1N) I))
L2 374 S L1 AND EMPTY
L3 106 S L2 AND (SUPPORT OR MATRIX OR BEAD)
L4 82 DUP REM L3 (24 DUPLICATES REMOVED)

=> s luxemburg A?/au or jackson M?/au or Peter ?/au
L5 24364 LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER ?/AU

=> s luxemburg A?/au or jackson M?/au or Peter P?/au
L6 7162 LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER P?/AU

=> s l6 and (MHC and empty)
L7 8 L6 AND (MHC AND EMPTY)

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 5 DUP REM L7 (3 DUPLICATES REMOVED)

=> dis l8 1-5 ibib abs

L8 ANSWER 1 OF 5 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 95343344 MEDLINE
DOCUMENT NUMBER: 95343344 PubMed ID: 7542403
TITLE: Peptide binding and presentation by mouse CD1.
COMMENT: Comment in: Science. 1995 Jul 14;269(5221):185-6
AUTHOR: Castano A R; Tangri S; Miller J E; Holcombe H R; **Jackson M R**; Huse W D; Kronenberg M; Peterson P A
CORPORATE SOURCE: Department of Immunology, La Jolla, CA 92037, USA.
SOURCE: SCIENCE, (1995 Jul 14) 269 (5221) 223-6. Journal code: UJ7; 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950905
Last Updated on STN: 19960129
Entered Medline: 19950822

AB CD1 molecules are distantly related to the major histocompatibility complex (**MHC**) class I proteins. They are of unknown function. Screening random peptide phage display libraries with soluble **empty** mouse CD1 (mCD1) identified a peptide binding motif. It consists of three anchor positions occupied by aromatic or bulky hydrophobic amino acids. Equilibrium binding studies demonstrated that mCD1 binds peptides containing the appropriate motif with relatively high affinity. However, in contrast to classical **MHC** class I molecules, strong binding to mCD1 required relatively long peptides. Peptide-specific, mCD1-restricted T cell responses can be raised, which suggests that the findings are of immunological significance.

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:214787 CAPLUS
DOCUMENT NUMBER: 120:214787
TITLE: In vivo regulation of the assembly and intracellular transport of class I major histocompatibility complex molecules
AUTHOR(S): Song, Elizabeth S.; Yang, Young; **Jackson, Michael R.**; Peterson, Per A.
CORPORATE SOURCE: Dep. Immunol., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: J. Biol. Chem. (1994), 269(9), 7024-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using H-2Kb-transfected Balb/c 3T3 cells which generate "**empty**" H-2Kb mols. devoid of antigenic peptides, the authors show that peptide availability dets. the stability of class I mols. and dictates the overall intracellular transport rate of the class I complexes. The authors' data also indicate that chaperonin-like proteins are involved in class I assembly. Using Drosophila cells transfected with H-2Kb and murine .beta.2-microglobulin, the authors show that one possible candidate, calnexin, assocs. with class I mols. prior to peptide acquisition. These data suggest that both peptide supply and assembly proteins dictate cell surface expression of class I major histocompatibility complex mols. and

ultimately influence T cell recognition. The role of .beta.2-microglobulin in class I assembly is also discussed.

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:610306 CAPLUS
DOCUMENT NUMBER: 117:210306
TITLE: In vitro peptide binding to soluble **empty** class I major histocompatibility complex molecules isolated from transfected Drosophila melanogaster cells
AUTHOR(S): Matsumura, Masazumi; Saito, Yutaka; **Jackson, Michael R.**; Song, Elizabeth S.; Peterson, Per A.
CORPORATE SOURCE: Dep. Immunol., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: J. Biol. Chem. (1992), 267(33), 23589-95
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A sol. form of a mouse class I major histocompatibility antigen (H-2Kb) has been expressed in transfected D. melanogaster cells. These mols. were efficiently secreted (up to 4 mg/L) as noncovalent heterodimers and purified to homogeneity from cell supernatants. The isolated sol. Kb mols. were devoid of endogenous peptides. Using these mols., the authors characterized the Kb heavy chain-.beta.2-microglobulin (.beta.2m) assembly as well as peptide binding in vitro. In detergent-free soln. the heavy chains readily re-assembled with .beta.2m even in the absence of peptides. Kinetic analyses showed that the peptide binding is rapid and reversible and dependent on the heavy chains being assembled with .beta.2m. Likewise, peptide dissocd. from Kb mols. without the displacement of .beta.2m. Equil. binding expts. using various peptides confirmed that octapeptides bind to Kb mols. with the highest affinity and form the most stable complexes. However, in contrast to earlier studies, the N-terminal positioning of peptide to Kb mols. was more crucial than the C-terminal positioning and amidation of the peptide carboxylate did not affect the binding. Sol. Kb mols. could selectively bind allele-specific peptides among a mixt. of randomly synthesized octapeptides in vitro; however, no dominant residue was obsd. at the C terminus of bound peptides. Thus, the previously obsd. hydrophobic residues at the C terminus of peptides may reflect the specificity of enzyme(s) or protein(s) involved in peptide processing in vivo.

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:78915 CAPLUS
DOCUMENT NUMBER: 118:78915
TITLE: **Empty** and peptide-containing conformers of class I major histocompatibility complex molecules expressed in Drosophila melanogaster cells
AUTHOR(S): **Jackson, Michael R.**; Song, Elizabeth S.; Yang, Youngg A.; Peterson, Per A.
CORPORATE SOURCE: Dep. Immunol., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1992), 89(24), 12117-21
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Transfected D. melanogaster cells can express large quantities of class I major histocompatibility complex mols. Such mols. lack endogenous peptides because the Drosophila cells are devoid of proteins necessary for intracellular peptide loading. The **empty** mols. are efficiently expressed on the cell surface and can acquire extracellular peptides. The conformation and stability of **empty** murine class I mols. are detd. by the source of .beta.2-microglobulin. All .beta.2-microglobulin-induced conformers of **empty** heavy chains seem to be unified in a common rigid conformation on peptide binding.

L8 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:318170 BIOSIS
DOCUMENT NUMBER: BR43:18895
TITLE: EXPRESSION OF **EMPTY MHC** CLASS I IN INSECT CELLS.
AUTHOR(S): **JACKSON M R**; SONG E; YANG Y; PETERSON P A
CORPORATE SOURCE: DEP. IMMUNOL., SCRIPPS RES. FOUND., LA JOLLA, CALIF. 92037.
SOURCE: KEYSTONE SYMPOSIUM ON ANTIGEN PRESENTATION FUNCTIONS OF THE MHC (MAJOR HISTOCOMPATIBILITY COMPLEX), TAOS, NEW MEXICO, USA, MARCH 5-11, 1992. J CELL BIOCHEM SUPPL, (1992) 0 (16 PART D), 15.
CODEN: JCBSD7.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

=> dis his

(FILE 'HOME' ENTERED AT 12:52:53 ON 16 APR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 12:53:02 ON 16 APR 2002
L1 41486 S (MHC AND (CLASS (1N) I))
L2 374 S L1 AND EMPTY
L3 106 S L2 AND (SUPPORT OR MATRIX OR BEAD)
L4 82 DUP REM L3 (24 DUPLICATES REMOVED)
L5 24364 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER ?/AU
L6 7162 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER P?/AU
L7 8 S L6 AND (MHC AND EMPTY)
L8 5 DUP REM L7 (3 DUPLICATES REMOVED)

=> dis l4 1-10 kwic

L4 ANSWER 1 OF 82 MEDLINE
AB Tapasin retains **empty** or suboptimally loaded **MHC class I** molecules in the endoplasmic reticulum (ER). However, the molecular mechanism of this process and how tapasin itself is retained in. . .
CT Check Tags: Human; **Support**, U.S. Gov't, P.H.S.
ATP-Binding Cassette Transporters: ME, metabolism
Antiporters: GE, genetics
*Antiporters: ME, metabolism
Bacterial Proteins: GE, genetics
Bacterial Proteins:. . .

L4 ANSWER 2 OF 82 MEDLINE
AB CD1 is an **MHC class** I-like

antigen-presenting molecule consisting of a heavy chain and beta(2)-microglobulin light chain. The in vitro refolding of synthetic **MHC class I** molecules has always required the presence of ligand. We report here the use of a folding method using an immobilized. . . efficient assembly of ligand-free and ligand-associated CD1a and CD1b, starting with material synthesized in Escherichia coli. The results suggest that "**empty**" **MHC class I**-like molecules can assemble and remain stable at physiological temperatures in the absence of ligand. The use of oxidative refolding chromatography. . .

CT Check Tags: Human; **Support**, Non-U.S. Gov't
Antigens, CD1: GE, genetics
*Antigens, CD1: ME, metabolism
Chromatography: MT, methods
Circular Dichroism
GroEL Protein: ME, metabolism
Ligands

. . .

L4 ANSWER 3 OF 82 MEDLINE

AB . . . peptides to preformed CTL lines. It demonstrates that presentation of exogenous peptides involves peptide uptake and loading onto newly synthesized **MHC class I** molecules. This mechanism was best demonstrated for low affinity peptides in the presence of irrelevant peptides competing for HLA binding. . . A significantly reduced the presentation of low affinity peptides. This was not restored by adding exogenous beta(2)-microglobulin to stabilize the **MHC** complex on the cell surface. In contrast, presentation of high affinity peptides was not sensitive to cycloheximide or brefeldin A,. . . presentation of high and low affinity peptides by TAP-competent cells. High affinity peptides can apparently compete with peptides in preloaded **MHC class I** molecules at the cell surface, whereas low affinity peptides require **empty MHC** molecules within cells. Accordingly, very high concentrations of exogenous low affinity peptides in conjunction with active **MHC class I** metabolism were required to allow successful presentation against a background of competing intracellular high affinity peptides in TAP-competent cells. These. . .

CT Check Tags: Comparative Study; Human; **Support**, Non-U.S. Gov't
*ATP-Binding Cassette Transporters: IM, immunology
*ATP-Binding Cassette Transporters: ME, metabolism
Amino Acid Sequence
*Antigen Presentation: PH, physiology
Binding,. . . Cell Membrane: ME, metabolism
Dendritic Cells: CY, cytology
Dendritic Cells: IM, immunology
Dendritic Cells: ME, metabolism
HLA-A2 Antigen: ME, metabolism
Histocompatibility Antigens Class I: ME, metabolism
Interferon Type II: BI, biosynthesis
Intracellular Fluid: IM, immunology
Intracellular Fluid: ME, metabolism
Kinetics

. . .

CN 0 (ATP-Binding Cassette Transporters); 0 (HLA-A2 Antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Melan-A protein); 0 (Neoplasm Proteins); 0 (Peptides); 0 (RING4 protein)

L4 ANSWER 4 OF 82 MEDLINE DUPLICATE 1

AB H2-M3 is a class Ib **MHC** molecule that binds a highly restricted pool of peptides, resulting in its intracellular retention under normal conditions. However, addition of. . . features of M3 make it a powerful and novel model system to study the potentially interrelated functions of the ER-resident **class I** chaperone tapasin. The functions ascribed to tapasin include: 1) ER retention of peptide-**empty class I** molecules, 2) TAP stabilization resulting in increased peptide transport, 3) direct facilitation of peptide binding by **class I**, and 4) peptide editing. We report in this study that M3 is associated with the peptide-loading complex and that incubation. . . to define unique aspects of M3 biosynthesis, M3 was expressed in human cell lines that lack an M3 ortholog, but **support** expression of murine class Ia molecules. Unexpectedly, peptide-induced surface expression of M3 was observed in only one of two cell. . .

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
ATP-Binding Cassette Transporters: ME, metabolism
Adjuvants, Immunologic: DF, deficiency
Adjuvants, Immunologic: GE, genetics
Adjuvants, Immunologic: ME, metabolism

. . . PH, physiology
Cell Line, Transformed
Epitopes: CH, chemistry
Epitopes: GE, genetics
Epitopes: ME, metabolism
H-2 Antigens: ME, metabolism
Hela Cells
***Histocompatibility Antigens Class I: BI, biosynthesis**
***Histocompatibility Antigens Class I: CH, chemistry**
Histocompatibility Antigens Class I: GE, genetics
Histocompatibility Antigens Class I: ME, metabolism
Immunoglobulins: DF, deficiency
Immunoglobulins: GE, genetics
Immunoglobulins: ME, metabolism
*Immunoglobulins: PH, physiology
L Cells. . .

CN. . . 0 (ATP-Binding Cassette Transporters); 0 (Adjuvants, Immunologic); 0 (Antiporters); 0 (Epitopes); 0 (H-2 Antigens); 0 (H-2M3 antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Immunoglobulins); 0 (Peptides); 0 (RING4 protein); 0 (histocompatibility antigen H-2D(b)); 0 (tapasin)

L4 ANSWER 5 OF 82 MEDLINE

AB H2-M3 is a **MHC** class Ib molecule with a high propensity to bind N-formylated peptides. Due to the paucity of endogenous Ag, the majority. . . of N-formylated peptides onto the intracellular pool of M3. However, neither TAP nor tapasin is required for ER retention of **empty** M3.

CT Check Tags: Animal; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
ABC Transporters: GE, genetics
ABC Transporters: ME, metabolism
*ABC Transporters: PH, physiology

Antigen Presentation
Antiporters: GE, genetics
*Antiporters: PH, physiology
Binding, Competitive: IM, immunology
Cell Line, Transformed
Endoplasmic Reticulum: IM, immunology
Endoplasmic Reticulum: ME, metabolism
Histocompatibility Antigens Class I: ME, metabolism
Histocompatibility Antigens Class II: BI, biosynthesis
*Histocompatibility Antigens Class II: ME, metabolism
Immunoglobulins: DF,. . .
CN 0 (ABC Transporters); 0 (Antiporters); 0 (H2-M antigens); 0 (Histocompatibility Antigens **Class I**); 0 (Histocompatibility Antigens Class II); 0 (Immunoglobulins); 0 (Macromolecular Systems); 0 (Molecular Chaperones); 0 (Peptides); 0 (RING4 protein); 0 (beta. . .

L4 ANSWER 6 OF 82 MEDLINE
TI Accessory proteins that control the assembly of **MHC** molecules with peptides.
AB The stable assembly of Major Histocompatibility Complex (**MHC**) molecules with peptides is controlled by a number of cofactors, including proteins with general housekeeping functions and proteins with dedicated functions in **MHC** assembly. Recent work in my laboratory has focused on two chaperones, tapasin (tpn) and DM, that play critical roles in the loading of peptides onto **MHC class I** and **MHC** class II molecules, respectively. Tapasin is a transmembrane protein that tethers **empty class** I molecules in the endoplasmic reticulum to the transporter associated with antigen processing. DM is a peptide exchange factor that binds with **empty** and peptide-loaded class II molecules in endosomal and lysosomal compartments. Although a number of different functions for tapasin and DM have been proposed, emerging evidence suggests that both of these chaperones retain unstable **MHC** molecules in peptide-loading compartments until they bind with high-affinity peptides. These cofactors therefore promote the surface expression of long-lived **MHC**-peptide complexes.
CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
ATP-Binding Cassette Transporters: GE, genetics
ATP-Binding Cassette Transporters: PH, physiology
*Antigen Presentation: PH, physiology
Antiporters: DF, deficiency
Antiporters:. . . effects
Multienzyme Complexes: ME, metabolism
*Peptide Fragments: ME, metabolism
Protein Transport
Proteins: GE, genetics
Proteins: PH, physiology
Ribonucleoproteins: PH, physiology
Viral Matrix Proteins: GE, genetics
Viral Matrix Proteins: PH, physiology
CN. . . (Macromolecular Systems); 0 (Molecular Chaperones); 0 (Multienzyme Complexes); 0 (Peptide Fragments); 0 (Proteins); 0 (RING4 protein); 0 (Ribonucleoproteins); 0 (Viral **Matrix** Proteins); 0 (calreticulin); 0 (tapasin); EC 3.4.22 (Cysteine Endopeptidases); EC 3.4.99.46 (multicatalytic endopeptidase complex)

L4 ANSWER 7 OF 82 MEDLINE
TI Tapasin: an ER chaperone that controls **MHC class** I assembly with peptide.
AB The stable assembly of **MHC class I** molecules with peptides in the endoplasmic reticulum (ER) involves several accessory molecules. One of these accessory molecules is tapasin, a transmembrane protein that tethers **empty class I** molecules to the peptide transporter associated with antigen processing (TAP). Here, evidence is presented that tapasin retains **class I** molecules in the ER until they acquire high-affinity peptides.
CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
ABC Transporters: IM, immunology
*Antigen Presentation: IM, immunology
*Antiporters: IM, immunology
*Endoplasmic Reticulum: IM, immunology
***Histocompatibility Antigens Class I: IM, immunology**
*Immunoglobulins: IM, immunology
*Molecular Chaperones: IM, immunology
*Peptides: IM, immunology
CN 0 (ABC Transporters); 0 (Antiporters); 0 (Histocompatibility Antigens **Class I**); 0 (Immunoglobulins); 0 (Molecular Chaperones); 0 (Peptides); 0 (RING4 protein); 0 (tapasin)

L4 ANSWER 8 OF 82 MEDLINE
TI Macrophages present exogenous antigens by **class I** major histocompatibility complex molecules via a secretory pathway as a consequence of interferon-gamma activation.
AB Macrophages can process and present exogenous antigens on major histocompatibility complex (**MHC**) **class I** molecules through an alternative mechanism involving the internalization of antigens and the secretion of peptides loading **MHC class I** molecules at the cell surface. In this paper, we found that interferon-gamma (IFN-gamma) -activated macrophages infected with Salmonella typhimurum secreted peptides able to load **empty MHC** Kb molecules on co-cultured TAP-2-deficient RMA-S cells, added as targets for peptide loading. The increase in **class I** Kb on the RMA-S cells, resulting from the macrophage-derived peptides, exhibited a comparable stability as the direct addition of an. . . macrophages process exogenous antigens in an intracellular compartment where serine proteases generate peptides released to the external environment for loading **empty MHC class** I molecules at the cell surface. This TAP-independent mechanism for the **MHC class I** presentation may be involved in priming cytotoxic T lymphocytes against intracellular pathogens in vivo.
CT Check Tags: Animal; Female; **Support**, Non-U.S. Gov't
*Antigen Presentation: IM, immunology
Brefeldin A: PD, pharmacology
CD8-Positive T-Lymphocytes: IM, immunology
Cell Culture
Endosomes: IM, immunology
***Histocompatibility Antigens Class I: IM, immunology**
*Interferon Type II: IM, immunology
*Macrophage Activation: IM, immunology
Macrophages: DE, drug effects
*Macrophages: IM,. . .

CN 0 (Histocompatibility Antigens Class I); 0 (Peptides);
0 (Protein Synthesis Inhibitors)

L4 ANSWER 9 OF 82 MEDLINE
TI The structure and stability of an HLA-A*0201/octameric tax peptide complex with an empty conserved peptide-N-terminal binding site.
AB The crystal structure of the human class I MHC molecule HLA-A2 complexed with of an octameric peptide, Tax8 (LFGYPVYV), from human T cell lymphotrophic virus-1 (HTLV-1) has been determined.. .
.
CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't
Binding Sites: IM, immunology
Clone Cells
*Conserved Sequence
Crystallography, X-Ray
Cytotoxicity Tests, Immunologic
*Gene Products, tax: CH, chemistry
. . .

L4 ANSWER 10 OF 82 MEDLINE
AB Priming of cytotoxic T lymphocyte (CTL) activity with exogenous antigen requires introduction of the antigen into the MHC class I presentation pathway of antigen-presenting cells. In the present study, we used fusogenic reconstituted envelopes (virosomes), derived from influenza virus, as. . . influenza-specific CTLs generated through priming of mice with infectious virus. Intramuscular immunization of mice with peptide-containing virosomes induced a potent class I MHC-restricted CTL response against influenza-infected target cells. By contrast, an equal dose of NP-peptide encapsulated in fusion-inactivated virosomes did not induce. . . membrane fusion activity of the virosomes in the induction of the response. Likewise, NP-peptide encapsulated in liposomes, NP-peptide mixed with empty virosomes and NP-peptide in IFA failed to induce a CTL response. These results demonstrate that fusion-active virosomes represent a promising delivery system for induction of class I MHC -restricted CTL activity with non-replicating viral antigens.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Antigen-Presenting Cells: IM, immunology
CD4-Positive T-Lymphocytes: IM, immunology
CD8-Positive T-Lymphocytes: IM, immunology
Histocompatibility Antigens Class I: IM, immunology
Immunization
Mice
Mice, Inbred BALB C
*Nucleoproteins: IM, immunology
*Orthomyxoviridae: IM, immunology
Peptides: IM,. . .
CN 0 (Histocompatibility Antigens Class I); 0 (Nucleoproteins); 0 (Peptides); 0 (Viral Envelope Proteins)

=> dis l4 11-49 kwic

L4 ANSWER 11 OF 82 MEDLINE
TI Adenoviral-mediated gene transfer of ICP47 inhibits major histocompatibility complex class I expression on vascular cells in vitro.
AB . . . simplex gene ICP47 encodes a protein that binds to the host antigen-processing transporter, inhibiting the formation of major histocompatibility complex class I (MHC-I) antigens in infected cells. MHC-I antigen expression is also important in acute allograft rejection. This study was designed to quantitate the effect of adenoviral-mediated gene transfer of ICP47 on MHC-I cell surface expression of human vascular cells. We hypothesized that the transduction of vascular cells with a replication-incompetent adenoviral vector that was expressing ICP47 (AdICP47) would inhibit constitutive and inducible MHC-I expression and thereby reduce the rate of cytolysis of ICP47-transduced vascular cells by sensitized cytotoxic T lymphocytes (CTL). METHODS: A. . Cultured human vascular endothelial and smooth muscle cells and human dermal fibroblasts were transduced with either AdICP47 or the control empty vector AddlE1. Cell surface constitutive and gamma-interferon-induced MHC-I expression were quantitated by flow cytometry. A standard 4-hour chromium release cytotoxicity assay was used to determine the percent cytolysis. . . of transduced and nontransduced endothelial cells by sensitized CTL. Finally, to quantitate the specificity of the effect of ICP47 on MHC-I expression, adhesion molecule expression was quantitated in both transduced and nontransduced cells. RESULTS: Constitutive MHC-I expression in AdICP47-transduced endothelial cells was inhibited by a mean of 84% +/- 5% (SEM) in five experiments. After 48 hours of exposure to gamma-interferon, AdICP47-transduced cells exhibited a mean of 66% +/- 8% lower MHC -I expression than nontransduced cells. Similar inhibition in MHC -I expression was achieved in AdICP47-transduced vascular smooth muscle cells and dermal fibroblasts. Percent cytolysis of AdICP47-transduced endothelial cells by CTL was reduced by 72%. Finally, the specificity of the effect of transduction of ICP47 on vascular cell MHC-I expression was confirmed by a lack of significant change in either constitutive or tumor necrosis factor-induced vascular cell adhesion molecule/intercellular adhesion molecule expression. CONCLUSION: Transduction of vascular cells with AdICP47 strongly inhibits both constitutive and inducible MHC-I expression in human vascular cells. AdICP47-transduced cells exhibited a substantial reduction in cytolysis by CTL. Thus AdICP47 transduction holds promise as a technique to characterize the role of MHC-I expression in acute vascular allograft rejection in vivo and as a potential therapeutic intervention.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adenoviridae
Cell Line
Endothelium, Vascular: CY, cytology
Fibroblasts
*Gene Transfer Techniques
Genetic Vectors
Graft Rejection: IM, immunology
***Histocompatibility Antigens Class I: IM, immunology**
Immediate-Early Proteins
Muscle, Smooth, Vascular: CY, cytology
Simplexvirus: GE, genetics
Skin: CY, cytology
Transduction, Genetic
CN 0 (Genetic Vectors); 0 (Histocompatibility Antigens Class I); 0 (ICP47 protein, herpes simplex virus); 0 (Immediate-Early

Proteins)

L4 ANSWER 12 OF 82 MEDLINE DUPLICATE 2
TI Introduction of the haemagglutinin transmembrane region in the influenza virus **matrix** protein facilitates its incorporation into ISCOM and activation of specific CD8(+) cytotoxic T lymphocytes.
AB The gene encoding the influenza virus A **matrix** (MA) protein was cloned into the bacterial expression vector pMalC with and without the sequence encoding the transmembrane region of. . . (CTL) clone specific for the MA protein after incubation with rMAHA-ISCOM but not after incubation with rMA, rMAHA, rMA-ISCOM or **empty** ISCOM. The B-LCL was also lysed by the CTL clone after incubation with **empty** ISCOM mixed with the respective MA proteins. Incubation of ISCOM with the rMAHA protein proved to be the most efficient. . . of the proteasome inhibitors lactacystin or clasto-lactacystin beta-lactone to the B-LCL incubated with rMAHA-ISCOM or the MA proteins mixed with **empty** ISCOM dramatically decreased the lysis by the CD8(+) CTL clone. These results indicate that the addition of a hydrophobic anchor to hydrophilic proteins in combination with ISCOM facilitates their entry in the **MHC class I** processing and presentation pathway. This may be an attractive approach for the development of subunit vaccines aiming at the induction. . .
CT Check Tags: Human; In Vitro; **Support**, Non-U.S. Gov't
Antigen Presentation
Base Sequence
DNA Primers: GE, genetics
HLA-A2 Antigen
*Hemagglutinin Glycoproteins, Influenza Virus: GE, genetics
*Hemagglutinin Glycoproteins,. . . IP, isolation & purification
Lymphocyte Transformation
Recombinant Fusion Proteins: GE, genetics
Recombinant Fusion Proteins: IM, immunology
*T-Lymphocytes, Cytotoxic: IM, immunology
***Viral Matrix Proteins: GE, genetics**
***Viral Matrix Proteins: IM, immunology**
CN. . . Primers); 0 (HLA-A2 Antigen); 0 (Hemagglutinin Glycoproteins, Influenza Virus); 0 (ISCOMs); 0 (Influenza Vaccine); 0 (Recombinant Fusion Proteins); 0 (Viral **Matrix** Proteins); 0 (influenza virus membrane protein)

L4 ANSWER 13 OF 82 MEDLINE
AB . . . heavy chain (HC), beta(2)-microglobulin (beta(2)m) and antigenic peptide, is generally believed to be a prerequisite for the expression of HLA **class I** molecules at the cell surface in vivo. Therefore, a possible role in immunological processes for HC/beta(2)m complexes devoid of peptide. . . novel HLA-B*2705-transgenic rat model and monoclonal antibodies that distinguish between structurally different forms of HLA-B27 molecules, we demonstrate here that **class I** molecules which appear to lack antigenic peptides are expressed in abundance on a variety of cell types in lymphoid organs. These results imply a role for structurally diverse, possibly **empty**, **MHC** molecules in physiological T cell selection which has so far not been sufficiently appreciated.
CT Check Tags: Animal; Comparative Study; Human; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Animals, Transgenic
Antibodies, Monoclonal: ME, metabolism
B-Lymphocytes: IM, immunology
B-Lymphocytes: ME, metabolism
Cell Line
Cytokines:. . .

L4 ANSWER 14 OF 82 MEDLINE
TI HLA-F is a predominantly **empty**, intracellular, TAP-associated **MHC** class Ib protein with a restricted expression pattern.
AB HLA-F is currently the most enigmatic of the human **MHC**-encoded class Ib genes. We have investigated the expression of HLA-F using a specific Ab raised against a synthetic peptide corresponding. . . tonsil and fetal liver, a major site of B cell development. Thermostability assays suggest that HLA-F is expressed as an **empty** heterodimer devoid of peptide. Consistent with this, studies using endoglycosidase-H and cell surface immunoprecipitations also indicate that the overwhelming majority. . . that this does not result in concomitant cell surface expression. HLA-F associates with at least two components of the conventional **class I** assembly pathway, calreticulin and TAP. The unusual characteristics of the predicted peptide-binding groove together with the predominantly intracellular localization raise. . .
CT Check Tags: Human; **Support**, Non-U.S. Gov't
*ABC Transporters: ME, metabolism
Adult
Amino Acid Sequence
Antigen Presentation
Cell Line
Gene Expression Regulation: IM, immunology
*HLA Antigens: BI, biosynthesis
HLA Antigens: GE, genetics
*HLA Antigens: IP, isolation & purification
HLA Antigens: ME, metabolism
***Histocompatibility Antigens Class I: BI, biosynthesis**
Histocompatibility Antigens Class I: GE, genetics
***Histocompatibility Antigens Class I: IP, isolation & purification**
Histocompatibility Antigens Class I: ME, metabolism
Interferon Type II: PD, pharmacology
*Intracellular Fluid: IM, immunology
*Intracellular Fluid: ME, metabolism
Jurkat. . .
CN 0 (ABC Transporters); 0 (HLA Antigens); 0 (HLA-F antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Peptides); 0 (RING4 protein)

L4 ANSWER 15 OF 82 MEDLINE DUPLICATE 3
TI Distinct functions of tapasin revealed by polymorphism in **MHC class I** peptide loading.
AB Peptide assembly with **class I** molecules is orchestrated by multiple chaperones including tapasin, which bridges **class I** molecules with the TAP and is critical for efficient Ag presentation. In this paper, we show that, although constitutive levels. . . and efficient presentation of viral Ags to CTL. High levels of soluble murine tapasin, which do not bridge TAP and **class I** molecules, still restore normal surface expression of B*4402 in the tapasin-deficient human cell line 721.220.

These findings indicate distinct roles for tapasin in **class** I peptide loading. First, tapasin-mediated bridging of TAP-**class** I complexes, which despite being conserved across the human-mouse species barrier, is not necessarily sufficient for peptide loading. Second, tapasin mediates a function which probably involves stabilization of **empty class** I molecules and which is sensitive to structural compatibility of components within the loading complex. These discrete functions of tapasin predict. . .

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
ABC Transporters: ME, metabolism
Adjuvants, Immunologic: PH, physiology
Alleles
Antigen Presentation: GE, genetics
Antiporters: GE, genetics
Antiporters: ME,. . . Cell Membrane: ME, metabolism
HLA-B Antigens: BI, biosynthesis
HLA-B Antigens: GE, genetics
HLA-B Antigens: IM, immunology
HLA-B Antigens: ME, metabolism
Histocompatibility Antigens Class I: GE, genetics
Histocompatibility Antigens Class I: IM, immunology
***Histocompatibility Antigens Class I: ME, metabolism**
Immunoglobulins: GE, genetics
Immunoglobulins: ME, metabolism
*Immunoglobulins: PH, physiology
Mice
Mice, Inbred C3H
Mice, Inbred. . .

CN 0 (ABC Transporters); 0 (Adjuvants, Immunologic); 0 (Antiporters); 0 (HLA-B Antigens); 0 (HLA-B44); 0 (Histocompatibility Antigens **Class** I); 0 (Immunoglobulins); 0 (Peptides); 0 (RING4 protein); 0 (tapasin)

L4 ANSWER 16 OF 82 MEDLINE

TI Impaired assembly yet normal trafficking of **MHC class** I molecules in Tapasin mutant mice.

AB Loading of peptides onto major histocompatibility complex **class** I molecules involves a multifactorial complex that includes tapasin (TPN), a membrane protein that tethers **empty class** I glycoproteins to the transporter associated with antigen processing. To evaluate the in vivo role of TPN, we have generated Tpn mutant mice. In these animals, most **class** I molecules exit the endoplasmic reticulum (ER) in the absence of stably bound peptides. Consequently, mutant animals have defects in **class** I cell surface expression, antigen presentation, CD8+ T cell development, and immune responses. These findings reveal a critical role of TPN for ER retention of **empty class** I molecules. Tpn mutant animals should prove useful for studies on alternative antigen-processing pathways that involve post-ER peptide loading.

CT Check Tags: Animal; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
*Antigen Presentation: GE, genetics
*Antiporters: GE, genetics
Antiporters: IM, immunology
Biological Transport: GE, genetics
Biological Transport: IM, immunology
Gene Expression Regulation: IM, immunology
***Histocompatibility Antigens Class I: GE, genetics**
Histocompatibility Antigens Class I: IM, immunology
*Immunoglobulins: GE, genetics
Immunoglobulins: IM, immunology
Mice
Mutation

CN 0 (Antiporters); 0 (Histocompatibility Antigens **Class** I); 0 (Immunoglobulins); 0 (tapasin)

L4 ANSWER 17 OF 82 MEDLINE DUPLICATE 4

AB . . . (APCs). Currently available APCs often lead to significant background levels. It has been shown that transfected insect cells can express **empty MHC class** I molecules on their surface. We have transfected Drosophila melanogaster S2 cells and the Lepidopteran line Sf9 with the gene encoding. . . assay was assessed using CD8(+) T cells from HLA-A2.1(+) donors with known reactivity against an HLA-A2.1-binding epitope of the influenza **matrix** protein. Use of insect cells as APCs abrogated background spots, increasing sensitivity. We further observed that a short-term prestimulation of. . .

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
*Antigen-Presenting Cells: IM, immunology
Cell Culture
Cell Line
Drosophila melanogaster: CY, cytology
*Enzyme-Linked Immunosorbent Assay: MT, methods
. . . immunology
*Interferon Type II: AN, analysis
Interferon Type II: IM, immunology
Peptides: IM, immunology
Spodoptera: CY, cytology
Time Factors
Transfection
Viral Matrix Proteins: IM, immunology

CN 0 (HLA-A2 Antigen); 0 (Peptides); 0 (Viral **Matrix** Proteins); 0 (influenza virus membrane protein)

L4 ANSWER 18 OF 82 CAPLUS COPYRIGHT 2002 ACS

IT Histocompatibility antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**MHC** (major histocompatibility complex), **class** I, A and B and C, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Histocompatibility antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**MHC** (major histocompatibility complex), class II, complementation group A and B and C and D, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Proteins, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(cartilage oligomeric **matrix**, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Proteins, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**empty** spiracles homolog 1 and 2, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

L4 ANSWER 19 OF 82 CAPLUS COPYRIGHT 2002 ACS
IT Apolipoproteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(C-I, **core** group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Histocompatibility antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**MHC** (major histocompatibility complex), **class** I, A and B and C, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Histocompatibility antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**MHC** (major histocompatibility complex), class II, complementation group A and B and C and D, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Proteins, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cartilage oligomeric **matrix**, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Proteins, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**empty** spiracles homolog 1 and 2, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

L4 ANSWER 20 OF 82 MEDLINE DUPLICATE 5
AB RMA-S cells do not express functional TAP, yet they express **MHC class** I molecules at the cell surface, especially at reduced temperatures (26 degrees C). It is generally assumed that such **class** I molecules are "**empty**," devoid of any associated peptide. A radiochemical approach was used to label **class** I-associated peptides and to determine the extent to which Kb molecules in RMA-S cells are associated with peptides. These studies revealed. . . and presenting exogenously supplied OVA 257-264 peptide for presentation to CD8+ Kb-restricted T lymphocytes. Thus contrary to current models of **class** I assembly in TAP-deficient RMA-S cells, the presumably "**empty**" molecules are in fact associated with peptides at 26 degrees C. Together, our data **support** the existence of an alternative mechanism of peptide binding and display by **MHC class** I molecules in TAP-deficient cells that could explain their ability to present Ag.
CT Check Tags: Animal; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
*ABC Transporters: BI, biosynthesis
ABC Transporters: GE, genetics
*Antigen Presentation
Antigen Presentation: GE, genetics
Cytotoxicity Tests, Immunologic
. . .

L4 ANSWER 21 OF 82 MEDLINE
TI Definition and transfer of a serological epitope specific for peptide-**empty** forms of **MHC class** I.
AB Nascent **class** I molecules have been hypothesized to undergo a conformational change when they bind peptide based on the observation that most available antibodies only detect peptide-loaded **class** I. Furthermore recent evidence suggests that this peptide-facilitated conformational change induces the release of **class** I from association with transporter associated with antigen processing (TAP)/tapasin and other endoplasmic reticulum proteins facilitating **class** I assembly. To learn more about the structure of peptide-**empty class** I , we have studied mAb 64-3-7 that is specific for peptide-**empty** forms of L(d). We show here that mAb 64-3-7 detects a linear stretch of amino acids including principally residues 48Q and 50P. Furthermore, we demonstrate that the 64-3-7 epitope can be transferred to other **class** I molecules with limited mutagenesis. Interestingly, in the folded **class** I molecule residues 48 and 50 are on a loop connecting a beta strand (under the bound peptide) with the alpha(1). . . to propose that this loop is a hinge region. Importantly, the three-dimensional structure of this loop is strikingly conserved among **class** I molecules. Thus our findings suggest that all **class** I molecules undergo a similar conformational change in the loop around residues 48 and 50 when they associate with peptide.
CT Check Tags: Human; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antibodies, Monoclonal: IM, immunology
Cell Line
*Epitopes
Histocompatibility Antigens Class I: CH, chemistry
***Histocompatibility Antigens Class I: IM, immunology**
Molecular Sequence Data
Protein Conformation
Protein Folding
CN 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Histocompatibility Antigens **Class I**)

L4 ANSWER 22 OF 82 MEDLINE
AB . . . murine alloreactive cytotoxic T-cells to carry out their effector function has been investigated using target cells that express a unique **class** I major histocompatibility complex (**MHC**)-peptide pair. The human cell line T2 and the murine cell line RMA-S are defective in peptide transport components needed to effectively express stable **MHC class** I molecules at the cell surface. When T2 cells were infected with a vaccinia virus that encoded

the Kd gene and. . . cytotoxic T-lymphocytes (CTL). Similar results were obtained with the murine RMA-S-Kd cell line, transfected with cDNA able to express some '**empty**' Kd that is heat-labile. Adding another Kd-motif peptide from influenza virus haemagglutinin (HAP) stabilized the surface expression of Kd and. . . presence and absence of HAP peptide. Alloreactive CTL appear to have a more stringent requirement for a high density of **MHC class I** on cell surfaces relative to peptide-specific **MHC**-restricted CTL. We conclude that while Kd-restricted CTL activity is strictly peptide-specific, anti-Kd-specific alloreactivity is **MHC** allele-specific, but peptide-nonspecific. This conclusion is at odds with the Standard Model of T-cell receptor (TCR) function, but consistent with. . .

CT Check Tags: Animal; Human; **Support**, U.S. Gov't, P.H.S.
*Antigen Presentation
*Cytotoxicity, Immunologic
Histocompatibility Antigens Class I: IM, immunology
Isoantigens: IM, immunology
Mice
Mice, Inbred Strains
Peptides: IM, immunology
*T-Lymphocytes, Cytotoxic: IM, immunology

CN 0 (Histocompatibility Antigens **Class** I); 0 (Isoantigens); 0 (Peptides)

L4 ANSWER 23 OF 82 MEDLINE

AB The formation of a trimeric complex composed of **MHC class I** heavy chain, beta2-microglobulin (beta2m) and peptide ligand is a prerequisite for its efficient transport to the cell surface. We have. . . demonstrate that cell surface expression of HLA-E in mouse cells strictly depends on the coexpression of hbeta2m and that soluble **empty** complexes of HLA-E and hbeta2m display a low degree of thermostability. Both observations imply that low affinity interaction of HLA-E. . .

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
Alleles
Antigen Presentation: GE, genetics
*Antigen Presentation: IM, immunology
Gene Expression Regulation: IM, immunology
HLA Antigens: GE, genetics
*HLA Antigens: IM, immunology
Histocompatibility Antigens Class I: GE, genetics
***Histocompatibility Antigens Class I: IM, immunology**
Mice
Multiple Myeloma: GE, genetics
Multiple Myeloma: IM, immunology
Transfection
Tumor Cells, Cultured
beta 2-Microglobulin:. . .

CN 0 (HLA Antigens); 0 (HLA-E antigen); 0 (Histocompatibility Antigens **Class I**); 0 (beta 2-Microglobulin)

L4 ANSWER 24 OF 82 MEDLINE

AB . . . of diphtheria toxin (DTA) as a marker. We found that positively charged liposomes encapsulating DTA are cytotoxic to macrophages, while **empty** positively charged liposomes, DTA in negatively charged and neutral liposomes are not. Consistent with this, only macrophages pulsed with OVA in positively charged liposomes could significantly stimulate OVA-specific, **class I MHC**-restricted T cell hybridoma. These results suggest that the positively charged liposomes can deliver proteinaceous antigens efficiently into the cytoplasm of the macrophages/antigen-presenting cells, where the antigens are processed to be presented by **class I MHC** molecules to induce the cell-mediated immune response. Possible development of the safe and effective vaccine is discussed.

CT Check Tags: Animal; Female; **Support**, Non-U.S. Gov't
*Adjuvants, Immunologic: AD, administration & dosage
Antigen Presentation
*Liposomes: AD, administration & dosage
Mice
Mice, Inbred BALB C

. . .

L4 ANSWER 25 OF 82 MEDLINE

AB HLA-DM catalyzes the release of invariant chain fragments from newly synthesized major histocompatibility complex (**MHC**) class II molecules, stabilizes **empty** class II molecules, and edits class II-associated peptides by preferentially releasing those that are loosely bound. The ability of HLA-DM. . . pH 7. The structural basis for these properties of HLA-DM is unknown. Sequence homology suggests that HLA-DM resembles classical, peptide-binding **MHC** class II molecules. In this study, we examined whether HLA-DM has a secondary structure composition consistent with an **MHC** fold and whether HLA-DM changes conformation between pH 5 and pH 7. Far-UV circular dichroism (CD) spectra of recombinant soluble HLA-DM (sDM) indicate that HLA-DM belongs to the alpha/beta class of proteins and structurally resembles both **MHC class I** and **class** II molecules. The CD peak around 198 nm increases upon going from neutral to endosomal pH and drops sharply upon. . .

CT Check Tags: Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Circular Dichroism
Guanidine: PD, pharmacology
*HLA-D Antigens: CH, chemistry
HLA-D Antigens: DE, drug effects
HLA-D Antigens: GE,. . .

L4 ANSWER 26 OF 82 MEDLINE

AB The assembly of **MHC** Ia molecules in the endoplasmic reticulum requires the presence of peptide ligands and beta2m and is facilitated by chaperones in an ordered sequence of molecular interactions. A crucial step in this process is the interaction of the **class I** alpha-chain/beta2m dimer with TAP, which is believed to ensure effective peptide loading of the **empty class I** molecule. We have previously demonstrated impaired intracellular transport of the class Ib molecule HLA-E in mouse myeloma cells cotransfected with. . . to enhance cell surface expression of HLA-E. Peptide binding was confirmed by testing the effect on the thermostability of soluble **empty** HLA-E/human beta2m dimers. Two viral peptides binding to HLA-E were thus identified, for which the exact positioning of the N. . .

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
Amino Acid Sequence

*Antigen Presentation
*Carrier Proteins: IM, immunology
Flow Cytometry
*HLA Antigens: IM, immunology
*Histocompatibility Antigens Class I: IM, immunology
Mice
Molecular Sequence Data
*Peptides: IM, immunology
Precipitin Tests
Tumor Cells, Cultured
CN 0 (Carrier Proteins); 0 (HLA Antigens); 0 (HLA-E antigen); 0 (Histocompatibility Antigens Class I); 0 (Peptides); 0 (tapasin)

L4 ANSWER 27 OF 82 MEDLINE
TI NK cells can recognize different forms of class I MHC.
AB NK recognition and lysis of targets are mediated by activation receptor(s) whose effects may be over-ridden by inhibitory receptors recognizing class I MHC on the target. Incubation of normal lymphoblasts with a peptide that can bind to their class I MHC renders them sensitive to lysis by syngeneic NK cells. By binding to class I MHC, the peptide alters or masks the target structure recognized by an inhibitory NK receptor(s). This target structure is most likely an "empty" dimer of class I heavy chain and beta2m as opposed to a "full" class I trimer formed by binding of specific peptide that is recognized by CTL.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
Antibiotics, Macrolide: PD, pharmacology
Antigens, Surface: ME, metabolism
Brefeldin A
Concanavalin A: PD, pharmacology
Cyclopentanes: PD, pharmacology
Cytotoxicity Tests, Immunologic
Cytotoxicity, Immunologic: DE, drug effects
H-2 Antigens: ME, metabolism
Histocompatibility Antigens Class I: BI, biosynthesis
Histocompatibility Antigens Class I: DE, drug effects
*Histocompatibility Antigens Class I: ME, metabolism
Killer Cells, Natural: DE, drug effects
*Killer Cells, Natural: IM, immunology
Killer Cells, Natural: ME,. . .
CN 0 (Antibiotics, Macrolide); 0 (Antigens, Surface); 0 (Cyclopentanes); 0 (H-2 Antigens); 0 (Histocompatibility Antigens Class I); 0 (Ly-49 antigen); 0 (Membrane Glycoproteins); 0 (Peptide Fragments); 0 (Protein Synthesis Inhibitors); 0 (Receptors, Immunologic); 0 (killer inhibitory receptor)

L4 ANSWER 28 OF 82 MEDLINE
AB . . . exogenous hepatitis B surface antigen (HBsAg) particles in an endolysosomal compartment generates peptides that bind to the major histocompatibility complex (MHC) class I molecule Ld and are presented to CD8+ cytotoxic T lymphocytes. Surface-associated 'empty' MHC class I molecules associated neither with peptide, nor with beta2-microglobulin (beta2m) are involved in this alternative processing pathway of exogenous antigen for MHC class I -restricted peptide presentation. Here, we demonstrate that internalization of exogenous beta2m is required for endolysosomal generation of presentation-competent, trimeric Ld molecules. . . . cells pulsed with exogenous HBsAg. These data point to a role of endocytosed exogenous beta2m in the endolysosomal assembly of MHC class I molecules that present peptides from endosomally processed, exogenous antigen.
CT Check Tags: Human; Support, Non-U.S. Gov't
*Antigen Presentation
*CD8-Positive T-Lymphocytes: IM, immunology
Cell Line
Epitopes: IM, immunology
*Hepatitis B Surface Antigens: IM, immunology
*Histocompatibility Antigens Class I: IM, immunology
*beta 2-Microglobulin: IM, immunology
CN 0 (Epitopes); 0 (Hepatitis B Surface Antigens); 0 (Histocompatibility Antigens Class I); 0 (beta 2-Microglobulin)

L4 ANSWER 29 OF 82 MEDLINE
TI Stability of empty and peptide-loaded class II major histocompatibility complex molecules at neutral and endosomal pH: comparison to class I proteins.
AB The structure and thermal stability of empty and peptide-filled forms of the murine class II major histocompatibility complex (MHC) molecule I-E(k) were studied at neutral and mildly acidic pH. The two forms have distinct circular dichroic spectra, suggesting that. . . change may accompany peptide binding. Thermal stability profiles indicate that binding of peptide significantly increases the thermal stability of the empty heterodimers at both neutral and mildly acidic pH. Free energies calculated from these data provide a direct measure of this stabilization and show that the empty form of I-E(k) is significantly more stable than that of class I MHC proteins. Furthermore, for the two MHC class II proteins that were analyzed (I-E(k) and I-A(d)), thermal stability was not significantly altered by acidification. In contrast, of four class I MHC molecules studied, three have shown a significant loss in complex stability at low pH. The marked stability exhibited by their empty form, as well as their resistance to low pH, as observed in this study, correlate well with the ability of class II MHC molecules to traverse and bind peptides in acidic endosomal vesicles.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
CHO Cells
Chimeric Proteins: BI, biosynthesis
Chimeric Proteins: CH, chemistry
Circular Dichroism
Endosomes: IM, immunology
HLA-A2 Antigen: CH, chemistry
HLA-B27 Antigen: CH, chemistry
Hamsters
Heat
*Histocompatibility Antigens Class I: CH, chemistry

Histocompatibility Antigens Class II: BI, biosynthesis
*Histocompatibility Antigens Class II: CH, chemistry
Hydrogen-Ion Concentration
Mice
. . .
CN 0 (Chimeric Proteins); 0 (HLA-A2 Antigen); 0 (HLA-B27 Antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Histocompatibility Antigens Class II); 0 (I-E-antigen); 0 (Peptide Fragments)

L4 ANSWER 30 OF 82 MEDLINE
AB Virally infected cells degrade intracellular viral proteins proteolytically and present the resulting peptides in association with major histocompatibility complex (**MHC**) **class I** molecules to CD8+ cytotoxic T lymphocytes (CTLs). These cells are normally prone to CTL-mediated elimination. However, several viruses have evolved. . . the transport of peptide antigens into the endoplasmatic reticulum, as shown in the TAP-specific peptide transporter assay, their loading onto **empty MHC** I molecules, and the subsequent translocation to the cell surface. As a consequence, IL-10 causes a general reduction of surface **MHC** I molecules on B lymphocytes that might also affect the recognition of EBV-infected cells by cytotoxic T cells.
CT Check Tags: Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
*B-Lymphocytes: ME, metabolism
Cell Membrane: ME, metabolism
Down-Regulation (Physiology)
Endoplasmic Reticulum: ME, metabolism
***Extracellular Matrix Proteins: ME, metabolism**
Herpesvirus 4, Human
Histocompatibility Antigens Class I: ME, metabolism
Immunosuppression
*Interleukin-10: PH, physiology
*Nerve Tissue Proteins: ME, metabolism
Peptide Fragments: ME, metabolism
Proteins: ME, metabolism
RNA, Messenger: GE, genetics
Recombinant Proteins
Viral Matrix Proteins: ME, metabolism
*Viral Proteins: PH, physiology
CN 0 (BCRF1 protein); 0 (EBV-associated membrane antigen); 0 (Extracellular **Matrix** Proteins); 0 (Histocompatibility Antigens **Class I**); 0 (LMP7 protein); 0 (Nerve Tissue Proteins); 0 (Peptide Fragments); 0 (Proteins); 0 (RNA, Messenger); 0 (Recombinant Proteins); 0 (Viral **Matrix** Proteins); 0 (Viral Proteins); 0 (terminal anchorage protein)

L4 ANSWER 31 OF 82 MEDLINE
TI The active site of ICP47, a herpes simplex virus-encoded inhibitor of the major histocompatibility complex (**MHC**)-encoded peptide transporter associated with antigen processing (TAP), maps to the NH2-terminal 35 residues.
AB . . . simplex virus (HSV) immediate early protein ICP47 inhibits the transporter associated with antigen processing (TAP)-dependent peptide translocation. As a consequence, **empty** major histocompatibility complex (**MHC**) **class I** molecules are retained in the endoplasmic reticulum and recognition of HSV-infected cells by cytotoxic T lymphocytes is abolished. We chemically. . .
CT Check Tags: Animal; Human; **Support**, U.S. Gov't, P.H.S.
*ABC Transporters: AI, antagonists & inhibitors
Amino Acid Sequence
Base Sequence
Binding Sites
Biological Transport: DE, drug. . .

L4 ANSWER 32 OF 82 MEDLINE
AB . . . G418 selection and screened for IRF-1 mRNA expression by reverse transcriptase-PCR (RT-PCR). High expression clones had high levels of two **MHC class I** proteins (H-2Kb and H-2Db) on the cell surface that correlated with increased levels of **class I** mRNA by RT-PCR. Furthermore, these clones also had increased levels of **MHC** class II protein (I-Ab), which correlated with increased levels of one subunit of class II mRNA by RT-PCR. IRF-1-expressing clones. . . also demonstrated greater tumor latency and slower tumor growth against subsequent challenge with untransfected cells compared with mice immunized with **empty** vector-transfected cells. These studies demonstrate a tumor suppressor effect of IRF-1, which acts in vivo through both partial reversion of. . .
CT Check Tags: Animal; Female; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Cell Adhesion
Cell Division
DNA-Binding Proteins: PH, physiology
*DNA-Binding Proteins: TU, therapeutic use
Gene Expression
Gene Transfer Techniques
Genes, MHC Class I
Genes, MHC Class II
H-2 Antigens: IM, immunology
Histocompatibility Antigens Class II: GE, genetics
Immunotherapy
*Interferon Type II: PH, physiology
. . .

L4 ANSWER 33 OF 82 MEDLINE
TI **MHC class I** presentation of live and heat-inactivated Sendai virus antigen in T2Kb cells depends on an intracellular compartment with endosomal characteristics.
AB . . . T2Kb cells has endosomal characteristics depending on cellular activities such as uptake, vesicular transport and intracellular-vesicular proteolysis. In addition, internalized '**empty**' Kb molecules derived from the T2Kb cell surface appeared to be involved in the presentation of SV antigen, as demonstrated. . . and anti-Kb antibodies. The results thus indicate that T2Kb cells process SV antigen in an endosomal-like compartment which contain recycling '**empty**' Kb molecules.
CT Check Tags: Animal; Female; **Support**, Non-U.S. Gov't
Amines: PD, pharmacology
Antibodies, Monoclonal
*Antigen Presentation
Antigen Presentation: DE, drug effects
*Antigens, Viral
Cell Compartmentation

Cell Line
. . .

L4 ANSWER 34 OF 82 MEDLINE
TI An improved assembly assay for peptide binding to HLA-B*2705 and H-2K(k) **class I MHC** molecules.
AB The assembly assay for peptide binding to **class I** major histocompatibility complex (**MHC**) is based on the ability to stabilise **MHC class I** molecules from mutant cell lines by the addition of suitable peptides. Such cell lines lack a functional transporter associated with antigen presentation (TAP) and as a result accumulate **empty**, unstable **class** I molecules in the ER. These dissociate rapidly in cell lysates unless they are stabilised by the addition of an appropriate binding peptide during lysis. The extent of stabilisation of **class** I molecules is directly related to the binding affinity of the added peptide. However, some **MHC class I** molecules, including HLA-B * 2705 and H-2Kk are unusually stable in their peptide-receptive state making them inappropriate for analysis using this assay or assays which depend on the ability of peptides to stabilise **MHC class** I molecules at the cell surface. Here we present an improved method that permits reliable measurements of peptide binding to such **class I MHC** molecules that are unusually stable in the absence of peptide. Cells are lysed in the presence of peptide and incubated at 4 degrees C. After 2 h, during which peptide binding to **empty MHC** molecules occurs, the lysate is heated to a temperature which preferentially destabilises those **MHC** molecules that remain **empty**. We have used this technique to assay peptide binding to HLA-B * 2705, as well as to the murine allele. . .
CT Check Tags: Human; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Cell Line
Epitopes
*H-2 Antigens: ME, metabolism
*HLA-B Antigens: ME, metabolism
*Oligopeptides: ME, metabolism
Phenotype
. . .

L4 ANSWER 35 OF 82 MEDLINE
TI Peptide interaction with a **class I** major histocompatibility complex-encoded molecule: allosteric control of the ternary complex stability.
AB Thermodynamics and kinetics of interaction between a soluble **class I MHC** heterodimer composed of the H-2Kd heavy chain (H) and human beta 2microglobulin (beta 2m) with a dansylated peptide series based. . . three components produce a system which is stable as a trimer. This behavior is rationalized by the functional requirements of **class I** molecules: Peptide structure determines the ternary complex's lifetime, and peptide rebinding on the cell surface is rendered unlikely by the limited stability of the **empty** heterodimers and the very low peptide affinity of the heavy chains.
CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
Allosteric Regulation
CHO Cells
*H-2 Antigens: ME, metabolism
Hamsters
Kinetics
Nucleoproteins: ME, metabolism
Orthomyxoviridae: ME, metabolism
*Peptides: ME,. . .

L4 ANSWER 36 OF 82 MEDLINE
TI The natural killer cell receptor Ly-49A recognizes a peptide-induced conformational determinant on its major histocompatibility complex **class I** ligand.
AB Natural killer (NK) cells are inhibited from killing cellular targets by major histocompatibility complex (**MHC**) **class I** molecules. In the mouse, this can be mediated by the Ly-49A NK cell receptor that specifically binds the H-2Dd **MHC class** I molecule, then inhibits NK cell activity. Previous experiments have indicated that Ly-49A recognizes the alpha 1/alpha 2 domains of **MHC class I** and that no specific **MHC** -bound peptide appeared to be involved. We demonstrate here that alanine-substituted peptides, having only the minimal anchor motifs, stabilized H-2Dd expression. . . NK cells. Peptide-induced resistance was blocked only by an mAb that binds a conformational determinant on H-2Dd. Moreover, stabilization of "**empty**" H-2Dd heavy chains by exogenous beta 2-microglobulin did not confer resistance. In contrast to data for **MHC class I**-restricted T cells that are specific for peptides displayed **MHC** molecules, these data indicate that NK cells are specific for a peptide-induced conformational determinant, independent of specific peptide. This fundamental distinction between NK cells and T cells further implies that NK cells are sensitive only to global changes in **MHC class I** conformation or expression, rather than to specific pathogen-encoded peptides. This is consistent with the "missing self" hypothesis, which postulates that NK cells survey tissues for normal expression of **MHC class I**.
CT Check Tags: Animal; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
ABC Transporters: ME, metabolism
Amino Acid Sequence
Binding Sites
Cell Line
H-2 Antigens: BI, biosynthesis
H-2 Antigens:. . .

L4 ANSWER 37 OF 82 MEDLINE
TI pH dependence of **MHC class I**-restricted peptide presentation.
AB The function of **MHC class I** molecules is to bind and present antigenic peptides to cytotoxic T cells. Here, we report that **class I**-restricted peptide presentation is strongly pH dependent. The presentation of some peptides was enhanced at acidic pH, whereas the presentation of others was inhibited. Biochemical peptide-**MHC class I** binding assays demonstrated that peptide-**MHC class I** complexes are more stable at neutral pH than at acidic pH. We suggest that acid-dependent peptide dissociation can generate **empty** **class I** molecules and that the resulting binding potential can be exploited by a subset of peptide-**MHC**

class I combinations, in some cases leading to considerable peptide exchange. We further speculate that the relative instability of peptide-class I complexes under acidic conditions may affect the outcome of class I -restricted Ag presentation, as less stably associated peptides may dissociate from class I during passage of the acidic trans-Golgi network, and therefore may not be presented. Finally, our results may in part explain how endocytosed proteins can be presented by MHC class I molecules to cytotoxic T cells.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
*Antigen Presentation: PH, physiology
*Histocompatibility Antigens Class I: ME, metabolism
Hybridomas
Hydrogen-Ion Concentration
Kinetics
Mice
Molecular Sequence Data
*Peptides: IM, immunology
Peptides: ME, metabolism
Protein. . .

CN 0 (Histocompatibility Antigens Class I); 0 (Peptides)

L4 ANSWER 38 OF 82 MEDLINE

TI 'Empty' Ld molecules capture peptides from endocytosed hepatitis B surface antigen particles for major histocompatibility complex class I-restricted presentation.

AB Peptides recognized by CD8+ cytotoxic T lymphocytes in the context of major histocompatibility complex (MHC) class I molecules are usually derived from endogenous proteins synthesized within the cell. Exogenous 22-nm hepatitis B surface antigen (HBsAg) particles are taken up by many cells, and are processed in a novel peptide-transporter-independent, endosomal or lysosomal pathway for class I (Ld)-restricted epitope presentation. Here, we present evidence that 'empty' Ld molecules derived from the cell surface are involved in presenting antigenic peptides from endocytosed HBsAg particles. Intracellular assembly of presentation-competent, trimeric Ld molecules required endocytosis of the exogenous antigen and ' empty' Ld molecules. These data assign a functional role to surface-associated, 'empty' MHC class I molecules.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Antigen Presentation
Antigen Presentation: GE, genetics
*H-2 Antigens: GE, genetics
*H-2 Antigens: ME, metabolism
*Hepatitis B Surface Antigens:. . .

L4 ANSWER 39 OF 82 MEDLINE

TI Induction of functional empty class I major histocompatibility complex glycoproteins by photoactivated 8-methoxypsoralen.

AB . . . lyse tumor cells via T-cell receptor recognition of distinctive peptide antigens presented in the context of surface major histocompatibility complex class I (MHC class I) glycoproteins. Several human and experimental animal tumors express distinctive MHC class I -associated peptides, which can be selectively targeted by specific CD8+ CTLs. Malignant cells expressing low quantities of these peptides are poor inducers of CTL responses. Therefore, we have developed a method of externally loading increased amounts of antigenic peptides onto MHC class I molecules. In order to induce " empty" fillable MHC class I molecules capable of binding antigenic peptides, we exposed transformed murine T cells (RMA) to low dose (3 joules/cm2) ultraviolet A energy and 8-methoxypsoralen (100 ng per ml). Presence of "empty" class I molecules was ascertained by "meltdown" or loss of the thermodynamically unstable cold-induced "empty" molecules as identified by cytofluorography at 37 degrees C. Retained function of " empty" molecules was determined by their stabilization through addition of peptides of the correct size and sequence motif, prior to exposure. . .

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Cell Line
*Glycoproteins: ME, metabolism
*Histocompatibility Antigens Class I: ME, metabolism
*Methoxsalen: PD, pharmacology
Mice
*Photosensitizing Agents: PD, pharmacology
T-Lymphocytes, Cytotoxic: DE, drug effects
T-Lymphocytes, Cytotoxic:. . .

CN 0 (Glycoproteins); 0 (Histocompatibility Antigens Class I); 0 (Photosensitizing Agents)

L4 ANSWER 40 OF 82 MEDLINE

AB BACKGROUND: Glycoproteins encoded by the major histocompatibility complex class I region (MHC class I) present peptide antigens to cytotoxic T cells (CTLs). Peptides are delivered to the site of MHC class I assembly by the transporter associated with antigen processing (TAP), and cell lines that lack this transporter are unable to present endogenous antigens to CTLs. Although it has been shown that a fraction of newly synthesized class I molecules are in physical association with TAP, it is not known whether this interaction is functionally relevant, or where on the class I molecule the TAP binding site might be. RESULTS: C1R cells transfected with a mutant HLA-A2.1 heavy chain (HC), where threonine. . . CTLs. We have studied the biochemistry of this mutant in C1R cells, and found that a large pool of unstable empty class I HC-beta 2m (beta-2 microglobulin) heterodimers exist that are rapidly transported to the cell surface. The T134K mutant seemed to bind. . . presents intracellular antigen is associated with its inability to interact with the TAP heterodimer. CONCLUSIONS: These experiments establish that the class I-TAP interaction is obligatory for the presentation of peptide epitopes delivered to the endoplasmic reticulum (ER) by TAP. Wild-type HLA-A2.1 molecules. . . but is unstable, suggesting a role for the TAP complex as an intracellular checkpoint that only affects the release of class I molecules with stably bound peptide ligands.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*ABC Transporters: IM, immunology
Binding Sites
Biological Transport

Cell Line
Cell Membrane
HLA-A2 Antigen: GE, genetics
*HLA-A2 Antigen: IM, immunology
Histocompatibility Antigens Class I: IM, immunology
Immunoglobulins, Heavy-Chain: IM, immunology
*Major Histocompatibility Complex: IM, immunology
Phenotype
Point Mutation
Rabbits

CN 0 (ABC Transporters); 0 (HLA-A2 Antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Immunoglobulins, Heavy-Chain); 0 (RING4 protein)

L4 ANSWER 41 OF 82 MEDLINE

TI **MHC class I** phenotype and function of human beta 2-microglobulin transgenic murine lymphocytes.

AB . . . binding studies, Scatchard analyses and flow cytometry, it is concluded that exogenous h beta 2m does not bind to hybrid **MHC class I** (**MHC**-I) molecules composed of mouse heavy chain/h beta 2m molecules expressed on lymphocytes of transgenic mice. Immunoprecipitation and SDS-PAGE analysis of metabolically labelled normal C57BL/6 lymph node cells showed binding of exogenous h beta 2m to **MHC**-I, in particular, to the H-2Db molecule through an exchange with endogenous mouse beta 2m. In contrast to normal H-2Db molecules,. . . peptide in the absence of exogenous added h beta 2m suggesting that a stable fraction of hybrid H-2Db molecules is **empty** or contain peptides with very low affinity. In a one-way allogenic mixed lymphocyte culture, transgenic splenocytes were found to be. . .

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
Antigens, Viral: IM, immunology
Flow Cytometry
*H-2 Antigens: IM, immunology
***Histocompatibility Antigens Class I: IM, immunology**
Lymph Nodes: CY, cytology
*Lymphocytes: IM, immunology
Mice
Mice, Inbred C57BL
Mice, Inbred DBA
Mice,. . .

CN 0 (Antigens, Viral); 0 (H-2 Antigens); 0 (Histocompatibility Antigens **Class I**); 0 (beta 2-Microglobulin); 0 (histocompatibility antigen H-2D(b))

L4 ANSWER 42 OF 82 MEDLINE

TI External glycopeptide binding to **MHC class-I** in relation to expression of TAP transporters, beta 2-microglobulin and to pH.

AB **MHC class-I** binding glycopeptides are easily visualized on the cell surface by carbohydrate specific monoclonal antibodies. By comparing the staining intensity between anti-carbohydrate and anti-**MHC class-I** specific monoclonal antibodies, an estimation of the fraction of peptide accessible ' **empty**' sites on the cell surface of **MHC class-**I molecules can be made. This system was used to analyze glycopeptide binding to **MHC class-I** molecules in relation to transporter associated with antigen processing (TAP) peptide transporters and beta 2-M expression, using gene targeted mice, and in relation to pH. Approximately 15, 40, and 95% '**empty** ' Db molecules were found on activated T cells from normal, beta 2-M-/- and TAP -/- mice, respectively. The ASN9-6h-Gal2 glycopeptide also bound to transfected '**empty**' Db molecules on T1-Db, T2-Db and T3-Db cells with a preference for T2-Db cells, lacking TAP peptide transporters. The stability. . . glycopeptides, binding either to Db or Kb. We conclude that external glycopeptide binding may reflect important functional properties in the **MHC class-I** system and that pH in different processing compartments might influence the expressed peptide repertoire.

CT Check Tags: **Support**, Non-U.S. Gov't
*ABC Transporters: BI, biosynthesis
ABC Transporters: GE, genetics
Biological Transport
Gene Targeting
*Glycoproteins: ME, metabolism
H-2 Antigens: IM, immunology
***Histocompatibility Antigens Class I: IM, immunology**
***Histocompatibility Antigens Class I: ME, metabolism**
Hydrogen-Ion Concentration
Lymphocyte Transformation
Peptide Fragments: IM, immunology
*T-Lymphocytes: IM, immunology
Tumor Cells, Cultured
. . .

CN 0 (ABC Transporters); 0 (Glycoproteins); 0 (H-2 Antigens); 0 (H-2k(b) antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Peptide Fragments); 0 (RING4 protein); 0 (beta 2-Microglobulin); 0 (histocompatibility antigen H-2D(b))

L4 ANSWER 43 OF 82 MEDLINE DUPLICATE 6

TI The interaction of beta 2-microglobulin (beta 2m) with mouse **class I** major histocompatibility antigens and its ability to **support** peptide binding. A comparison of human and mouse beta 2m.

AB The function of major histocompatibility complex (**MHC**) **class I** molecules is to sample peptides derived from intracellular proteins and to present these peptides to CD8+ cytotoxic T lymphocytes. In this paper, biochemical assays addressing **MHC class I** binding of both peptide and beta 2-microglobulin (beta 2m) have been used to examine the assembly of the trimolecular **MHC class I**/beta 2m/peptide complex. Recombinant human beta 2m and mouse beta 2ma have been generated to compare the binding of the two beta 2m to mouse **class I** . It is frequently assumed that human beta 2m binds to mouse **class I** heavy chain with a much higher affinity than mouse beta 2m itself. We find that human beta 2m only binds to mouse **class I** heavy chain with slightly (about 3-fold) higher affinity than mouse beta 2m. In addition, we compared the effect of the two beta 2m upon peptide binding to mouse **class I**. The ability of human beta 2m to **support** peptide binding correlated well with its ability to saturate mouse **class I** heavy chains. Surprisingly, mouse beta 2m only facilitated peptide binding when mouse beta 2m was used in excess (about 20-fold) of what was needed to saturate the **class I** heavy chains. The inefficiency of mouse beta 2m to **support** peptide binding could not be attributed to a

reduced affinity of mouse beta 2m/**MHC class I**
complexes for peptides or to a reduction in the fraction of mouse beta 2m/
MHC class I molecules participating in peptide
binding. We have previously shown that only a minor fraction of
class I molecules are involved in peptide binding,
whereas most of **class I** molecules are involved in beta
2m binding. We propose that mouse beta 2m interacts with the minor peptide
binding (i.e. the "**empty**") fraction with a lower affinity than
human beta 2m does, whereas mouse and human beta 2m interact with the
major. . . why mouse beta 2m is less efficient than human beta 2m in
generating the peptide binding moiety, and identifies the **empty**
MHC class I heavy chain as the molecule that
binds human beta 2m preferentially.

CT Check Tags: Animal; Comparative Study; Human; **Support**, Non-U.S.
Gov't
Amino Acid Sequence
Base Sequence
Binding Sites
***Histocompatibility Antigens Class I: ME, metabolism**
Mice
Molecular Sequence Data
Peptides: CH, chemistry
Peptides: ME, metabolism
Recombinant Proteins: ME, metabolism
*beta. . .

CN 0 (Histocompatibility Antigens **Class I**); 0 (Peptides);
0 (Recombinant Proteins); 0 (beta 2-Microglobulin)

L4 ANSWER 44 OF 82 CAPLUS COPYRIGHT 2002 ACS

TI Peptide influences the folding and intracellular transport of free major
histocompatibility complex **class** I heavy chains

AB **Class** I major histocompatibility complex mols. require
both .beta.2-microglobulin (.beta.2m) and peptide for efficient
intracellular transport. With the exception of H-2Db and Ld,
class I heavy chains have not been detectable at the
surface of cells lacking .beta.2m. The authors show that properly
conformed **class I** heavy chains can be detected in a
terminally glycosylated form indicative of cell surface expression H-2b,
H-2d, and H-2s .beta.2m-/-. . . demonstrate the presence of Kb mols. at
the surface of .beta.2m-/- cells cultured at 37.degree.. The mode of
assembly of **class I** mols. encompasses two major
pathways: binding of peptide to preformed "**empty**" heterodimers,
and binding of peptide to free heavy chains, followed by recruitment of
.beta.2m. In **support** of the existence of the latter pathway,
the authors provide evidence for a role of peptide in intracellular
transport of free **class I** heavy chains, through anal.
of Con A-stimulated splenocytes from transporter assocd. with antigen
processing 1 (TAP1)-/-, .beta.2m-/-, and double-mutant TAP1/.beta.2m-/-.
. .

ST peptide **MHC class I** antigen folding;
transport **MHC class I** peptide

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BIOL (Biological study); PROC (Process)
(folding and intracellular transport of free **MHC**
class I heavy chains in mouse splenocytes response
to)

IT Mouse
(peptide influences folding and intracellular transport of free
MHC class I heavy chains in splenocytes of)

IT Histocompatibility antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(H-2D, peptide influences folding and intracellular transport of free
MHC class I heavy chains in mouse
splenocytes)

IT Histocompatibility antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(H-2K, peptide influences folding and intracellular transport of free
MHC class I heavy chains in mouse
splenocytes)

IT Histocompatibility antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(H-2L, peptide influences folding and intracellular transport of free
MHC class I heavy chains in mouse
splenocytes)

IT Histocompatibility antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**MHC** (major histocompatibility antigen complex),
class I, peptide influences folding and intracellular
transport of free heavy chains in mouse splenocytes)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)
(TAP-1 (transporter in antigen processing 1), peptide influences
folding and intracellular transport of free **MHC class**
I heavy chains in mouse splenocytes)

IT Spleen
(splenocyte, mouse; peptide influences folding and intracellular
transport of free **MHC class I** heavy
chains)

IT Biological transport
(translocation, peptide influences folding and intracellular transport
of free **MHC class I** heavy chains in mouse
splenocytes)

IT Microglobulins
RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)
(.beta.2-, peptide influences folding and intracellular transport of
free **MHC class I** heavy chains in mouse
splenocytes)

L4 ANSWER 45 OF 82 MEDLINE

TI Tap-1 and Tap-2 gene therapy selectively restores conformationally
dependent HLA **Class I** expression in type I diabetic
cells.

AB . . . feature of patients with HLA class II-linked autoimmune disease
is an abnormally low density of conformationally correct, self-peptide
filled HLA **class I** molecules on the lymphocyte cell
surface. The transporters associated with antigen processing (Tap-1 and
Tap-2) are essential for normal **class I** expression and
presentation of intracellular peptides, and these genes are located within
the HLA class II region. The aims of this project were to determine if Tap
genes could be implicated in the defective **class I**

expression associated with IDDM by using a novel Epstein-Barr virus (EBV)-mediated gene transfer system to introduce a cloned, normal Tap-2 or Tap-1 gene into B cell lines from normal and IDDM patients and analyzing the effect on conformationally dependent **class I** expression. The results show that Tap-2 gene transfer in B cells from 40% of randomly selected IDDM patients increased expression of conformationally correct, cell-surface **class I** molecules to levels comparable with similarly treated B cells from normal control individuals. B cells from another 40% of IDDM. . . effects were specific because B cells from normal individuals did not respond to Tap-1 or Tap-2 gene transfer with increased **class I** expression, and B cells from IDDM patients responding to Tap-2 gene transfer did not respond to Tap-1 gene transfer and vice versa. Thus, these complementation studies identify distinct, non-overlapping subsets of IDDM patients whose **class I** defect in B cells can be reversed by Tap-1 or Tap-2 gene transfer. The increase in **class I** expression induced by Tap gene transfer is associated with a reduction in the number of peptide-**empty class I** molecules as demonstrated by the response to exogenous peptide loading. Furthermore, the increase in self-peptide filled **class I** molecules induced by Tap gene transfer into B cells from IDDM patients is associated with restored antigen presentation to autologous T cells. These studies conclude that Tap gene dysfunctions may contribute to the defect in **class I** phenotype and antigen presentation demonstrated by IDDM patients. Defective presentation of self-peptides by antigen presenting cells can lead to the. . .

CT Check Tags: Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
*ABC Transporters: GE, genetics
Amino Acid Sequence
Antigen Presentation
B-Lymphocytes
Base Sequence
Diabetes Mellitus, Insulin-Dependent: GE, genetics
*Diabetes Mellitus, Insulin-Dependent: IM, immunology
Diabetes Mellitus, Insulin-Dependent: TH, therapy
Gene Expression
*Gene Therapy
*Gene Transfer Techniques
***Genes, MHC Class II: GE, genetics**
Genetic Vectors: GE, genetics
Herpesvirus 4, Human: GE, genetics
***Histocompatibility Antigens Class I: BI, biosynthesis**
Histocompatibility Antigens Class I: CH, chemistry
Molecular Sequence Data
Peptides: CS, chemical synthesis
Peptides: ME, metabolism
Protein Conformation
RNA, Messenger:. . .

CN 0 (ABC Transporters); 0 (Genetic Vectors); 0 (Histocompatibility Antigens **Class I**); 0 (Peptides); 0 (RING4 protein); 0 (RNA, Messenger)

L4 ANSWER 46 OF 82 MEDLINE

AB Major histocompatibility complex (**MHC**) **class I** allele-specific binding motifs have proved useful in predicting cytotoxic T-cell epitopes from immunogenic proteins. In a search of the E6. . . motif, we discovered four potential binding peptides. One peptide, E6.1 (sequence 50-57, YDPAFRDL), was poor in its ability to stabilize **empty** Kb on RMA-S cells, with a t1/2 = 33 min versus 30 min for **empty** Kb. This peptide subsequently proved to be non-immunogenic upon mouse in vivo vaccination. It was hypothesized that an isoleucine for. . .

CT Check Tags: Animal; Female; **Support**, Non-U.S. Gov't
*Antigens, Neoplasm: IM, immunology
Base Sequence
Cell Line
DNA Primers: GE, genetics
H-2 Antigens: IM, immunology
***Histocompatibility Antigens Class I: IM, immunology**
*Immunization
Kinetics
Lymphocyte Transformation
Mice
Mice, Inbred C57BL
Molecular Sequence Data
Oncogene Proteins, Viral: GE,. . .

CN 0 (Antigens, Neoplasm); 0 (DNA Primers); 0 (H-2 Antigens); 0 (H-2k(b) antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Oncogene Proteins, Viral); 0 (Vaccines, Synthetic); 0 (Viral Vaccines); 0 (oncogene protein E6, human papillomavirus type 16)

L4 ANSWER 47 OF 82 MEDLINE

AB . . . and a nitrile analogue, representing cyclisation or dehydration of the asparagine residue. The candidate aspartimide and nitrile analogues both bound **empty MHC class I** molecules to form allo determinants recognised by monoclonal antibodies. These results demonstrate that altered synthetic peptides can bind **class I MHC** molecules and prompt caution in the use of synthetic peptides as a source of immunising antigen.

CT Check Tags: Animal; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Aspartic Acid: AA, analogs & derivatives
Cell Line
H-2 Antigens: IM, immunology
Indicators and Reagents
. . .

L4 ANSWER 48 OF 82 MEDLINE

AB CD1 molecules are distantly related to the major histocompatibility complex (**MHC**) **class I** proteins. They are of unknown function. Screening random peptide phage display libraries with soluble **empty** mouse CD1 (mCD1) identified a peptide binding motif. It consists of three anchor positions occupied by aromatic or bulky hydrophobic. . . binding studies demonstrated that mCD1 binds peptides containing the appropriate motif with relatively high affinity. However, in contrast to classical **MHC class I** molecules, strong binding to mCD1 required relatively long peptides. Peptide-specific, mCD1-restricted T cell responses can be raised, which suggests that. . .

CT Check Tags: Animal; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence

*Antigen Presentation
Antigens, CD: CH, chemistry
*Antigens, CD: IM, immunology
Antigens, CD: ME, metabolism
. . .

L4 ANSWER 49 OF 82 MEDLINE DUPLICATE 7
TI Evidence for an early heavy chain intermediate in the assembly of H-2Db **class I MHC** molecules.
AB Several recently proposed models for the in vivo biogenesis of **class I MHC** molecules focus on the retention of **empty** dimers as a postulated intermediate in the assembly of the complete complexes. The data presented in this study **support** a slightly different model of **class I** biogenesis, which includes a precursor population of H-2Db heavy chains (HCs) that is retained in the ER of murine cells. . . prior to its association with beta-2 microglobulin (beta 2m). For this study the intracellular ratios of the subunits that comprise **class I** molecules have been manipulated to generate a transfected cell line which assembles only very small numbers of unstable H-2Db molecules.. . . were not associated with beta 2m, has been detected. These immature HCs exhibited several characteristics of a precursor to complete **class I** molecules and required a supply of endogenously synthesized peptides for their normal processing in vivo.
CT Check Tags: Animal; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antibodies, Monoclonal: IM, immunology
Flow Cytometry
*H-2 Antigens: BI, biosynthesis
H-2 Antigens: CH, chemistry
. . .

=> dis l4 50-82 kwic

L4 ANSWER 50 OF 82 MEDLINE
TI Binding of diverse peptides to **MHC class I** molecules inhibits target cell lysis by activated natural killer cells.
AB **Class I MHC** expression by target cells inhibits lysis mediated by natural killer (NK) cells, often in an allele-specific fashion. It has been proposed that NK cell inhibitory receptors recognize complexes of **class I** molecules with specific cellular peptides that define self, displacement of which would render cells NK sensitive. By loading the mostly **empty** Dd **class I** molecules of cell lines deficient in peptide transporter molecules with synthetic or natural Dd-bound peptides, we have demonstrated specific dose-dependent inhibition of the Ly49+ subset of activated NK cells by **class I**-peptide complexes. Inhibition occurred with most if not all Dd-binding peptides, suggesting that Ly49+ NK cells recognize **class I**-peptide complexes largely independently of peptide composition. The results suggest a primary role of NK cells in the destruction of cells that have down-regulated or extinguished cell surface expression of some or all **class I** molecules.
CT Check Tags: Animal; **Support**, U.S. Gov't, P.H.S.
ABC Transporters: GE, genetics
*ABC Transporters: PH, physiology
Amino Acid Sequence
Biological Transport
Cell Line
*Cytotoxicity, Immunologic:. . .

L4 ANSWER 51 OF 82 MEDLINE
TI Major histocompatibility complex **class I** binding glycopeptides for the estimation of '**empty**' **class I** molecules.
AB Different forms of major histocompatibility complex (**MHC**) **class I** heavy chains are known to be expressed on the cell surface, including molecules which are functionally '**empty**'. Direct peptide binding to cells is obvious during sensitization of target cells in vitro for cytotoxic T lymphocyte killing and '**empty**' **MHC**-I molecules are comparatively abundant on TAP-1/2 peptide transporter mutant cells. In the present work we have estimated the fraction of '**empty**' **MHC class** I molecules using glycosylated peptides and cellular staining with carbohydrate specific monoclonal antibodies. Synthetic Db and Kb binding peptides were coupled. . . An optimal Db binding glycopeptide was used for comparative staining with anti-Db and anti-carbohydrate monoclonal antibodies to estimate fractions of '**empty**' molecules on different T lymphoid cells. On activated normal T cells, a large fraction of Db molecules were found to be '**empty**'. The functional role of such '**empty**' **MHC class I** molecules on T cells is presently unclear. However, on antigen presenting cells they might participate in the antigen presentation process.
CT Check Tags: Animal; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Antibodies, Monoclonal: CH, chemistry
Cell Line
Disaccharides: CH, chemistry
Disaccharides: IM, immunology
G(M3) Ganglioside: AA,. . .

L4 ANSWER 52 OF 82 MEDLINE
TI . . . Competition inhibition of cytotoxic T-lymphocyte (CTL) lysis, a more sensitive method to identify candidate CTL epitopes than induction of antibody-detected **MHC class I** stabilization.
AB We compared the efficiency of two commonly used cellular major histocompatibility complex (**MHC**) **class I** peptide-binding assays to identify a cytotoxic T lymphocyte (CTL) epitope-containing peptide among length variants derived from the human papilloma virus. . . differed markedly. In a peptide competition cytotoxicity (PCC) assay, based on inhibition of CTL lysis by competition for binding to **MHC class**-I molecules between a known CTL epitope-containing peptide and peptide of interest, E7 49-57 bound 45-fold more efficiently to Db than the second Db-binding peptide in line. In the widely used RMA-S **MHC class I** peptide-binding assay, based on peptide-induced stabilization of '**empty**' **MHC class**-I molecules at the surface of antigen-processing defective RMA-S cells, this difference was only 3 fold. Similar differences were observed when. . . for H-2Kb were analyzed in both assays. We conclude that the PCC assay discriminates more efficiently between high- and low-affinity **MHC class** I binding peptides than the RMA-S assay. This observation is

ascribed to the fact that peptide-**MHC class I**
dissociation is an important parameter in the PCC but not the RMA-S assay.
CT Check Tags: Animal; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Antigenic Variation
Binding, Competitive: IM, immunology
Cell Line
*Cytotoxicity, Immunologic
Epitope Mapping
*Epitopes: CH, chemistry
. . .

L4 ANSWER 53 OF 82 MEDLINE
TI Effects of peptide length and composition on binding to an **empty class I MHC** heterodimer.
AB **Class I** major histocompatibility complex (**MHC**
) proteins present peptide antigens to T cells during the immune response against viruses. Peptides are loaded into newly synthesized **class I** heterodimers in the endoplasmic reticulum such that most or all cell surface **class I** molecules contain peptides derived from endogenous or foreign proteins. We previously reported the assembly of **empty** heterodimers of the murine **class I MHC** molecule H-2Kd, from denatured heavy and light chains from which endogenous peptides had been removed [Fahnestock et al. (1992) Science 258, 1658-1662]. Here we measure thermal stability profiles of **empty** versus peptide-filled molecules and compare the effects of human versus murine light chains on the overall stability of the Kd heterodimer. The majority of **empty** heterodimers are stable at 37 degrees C regardless of the species of light chain, indicating that our previous report of. . . not due to use of a murine/human chimeric protein. Binding constants are derived for a series of peptides interacting with **empty** Kd heterodimers. The dissociation constants of four known Kd-restricted peptides range from 2.3 x 10(-7) to 3.4 x 10(-8) M.. . . affinity of one Kd-restricted peptide are explored, and the results are interpreted with reference to the known three-dimensional structures of **class I MHC** protein/peptide complexes.
CT Check Tags: Animal; Comparative Study; Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antigen Presentation
CHO Cells
*H-2 Antigens: CH, chemistry
H-2 Antigens: GE, genetics
H-2 Antigens:. . .

L4 ANSWER 54 OF 82 MEDLINE
AB The assembly of class Ia **MHC** Ags is thought to occur in the endoplasmic reticulum (ER) where H chains, beta 2m, and peptides come together to form trimers. Several types of proteins are implicated in the regulation of class Ia **MHC** assembly, including: 1) TAP1/TAP2 transporters, which translocate peptides derived from naturally processed endogenous proteins from the cytosol into the ER. . . and peptide-binding mechanisms. We find that in TAP2 negative RMA-S cells, the great majority of GPIQa-2 and SQa-2 behave as "**empty**" heterodimers: They cannot maintain stable conformations at 37 degrees C, but their half-lives can be significantly extended by reducing the. . . results suggest that the Qa-2 binding peptides are delivered to Qa-2 molecules in a manner similar to the class Ia **MHC** Ag system and, therefore, that both GPIQa-2 and SQa-2 may be assembled in the ER. Detection of a small population. . .
CT Check Tags: Human; **Support**, U.S. Gov't, P.H.S.
Biological Transport
*Carrier Proteins: PH, physiology
Cell Line
Endoplasmic Reticulum: ME, metabolism
*Glycosylphosphatidylinositols: PH, physiology
***Histocompatibility Antigens Class I: AN, analysis**
***Histocompatibility Antigens Class I: ME, metabolism**
Temperature
Transfection
CN 0 (Carrier Proteins); 0 (Glycosylphosphatidylinositols); 0 (Histocompatibility Antigens **Class I**); 0 (Q surface antigens)

L4 ANSWER 55 OF 82 MEDLINE
AB Cytotoxic T lymphocytes (CTL) recognize antigenic peptides presented by major histocompatibility complex **class I** (**MHC**
-I) molecules on the surface of target cells. Optimal induction of CD8+ CTL depends on the amount of relevant peptide/**MHC**-I complexes and the presence of co-stimulatory molecules on antigen-presenting cells (APC). The antigen-processing defective mutant cell line RMA-S, when cultured at low temperature, expresses high amounts of **MHC**-I molecules that do not contain endogenously derived peptides. These " **empty**" **MHC**-I molecules can be stabilized by addition of **MHC**-binding peptides. RMA-S cultured at low temperatures with selected peptides have been used for in vitro CTL induction with conflicting results.. . . priming. This system may also help to address the issue of the different contributions of co-stimulation and relative occupancy of **MHC**-I by single peptide epitopes in CTL priming.
CT Check Tags: Animal; Female; **Support**, Non-U.S. Gov't
Amino Acid Sequence
*Antigen-Presenting Cells: PH, physiology
Antigens, CD8: PH, physiology
Antigens, CD80: AN, analysis
Antigens, CD80: GE, genetics
*Antigens, CD80: PH, physiology
*Epitopes
Histocompatibility Antigens Class I: PH, physiology
Melanoma: IM, immunology
Mice
Molecular Sequence Data
Ovalbumin: IM, immunology
Peptide Fragments: IM, immunology
. . .
CN 0 (Antigens, CD8); 0 (Antigens, CD80); 0 (Epitopes); 0 (Histocompatibility Antigens **Class I**); 0 (Peptide Fragments)

L4 ANSWER 56 OF 82 MEDLINE
TI Major histocompatibility complex **class I** allele-specific peptide libraries: identification of peptides that mimic an H-Y T cell epitope.
AB . . . of random peptides for T cell antigens. Two libraries were

constructed, containing fixed amino acids representing the major histocompatibility complex (**MHC**) **class I** anchor residues for H-2Kb-restricted octamers and H-2Db-restricted nonamers. Peptides from the Kb-restricted library (KbL: SXIXFXXL) and the Db-restricted library (DbL: XXXXNXXXIM) specifically stabilize **empty** Kb and Db molecules, respectively. The libraries contain peptides that mimic several H-2b-restricted cytotoxic T lymphocyte epitopes, and 21 mimotopes. . . . high performance liquid chromatography analysis. This peptide is also capable of immunizing female mice against male splenocytes. Several applications for **MHC**-restricted peptide libraries are discussed.

CT Check Tags: Animal; Female; Male; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence
Base Sequence
*Epitopes: IM, immunology
Genomic Library
*H-Y Antigen: IM, immunology
Histocompatibility Antigens Class I: GE, genetics
***Histocompatibility Antigens Class I: IM, immunology**
Mice
Mice, Inbred C57BL
Molecular Sequence Data
*Peptides: IM, immunology
Recombinant Fusion Proteins: IM, immunology
. . .

CN 0 (Epitopes); 0 (H-Y Antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Peptides); 0 (Recombinant Fusion Proteins)

L4 ANSWER 57 OF 82 MEDLINE

TI Analysis of the structure of **empty** and peptide-loaded major histocompatibility complex molecules at the cell surface.

AB We compared the conformation of **empty** and peptide-loaded **class I** major histocompatibility complex (**MHC**) molecules at the cell surface. Molecular conformations were analyzed by fluorescence resonance energy transfer (FRET) between fluorescent-labeled Fab fragments bound to the alpha 2 domain of the **MHC** heavy chain and fluorescent-labeled Fab fragments bound to beta 2-microglobulin. No FRET was found between Fab fragments bound to **empty** H-2Kb, but FRET was detected when **empty** H-2Kb molecules were loaded with peptide. The magnitude of FRET depended on the sequence of the peptide used. The results imply that **empty** H-2Kb molecules are in a relatively extended conformation, and that this conformation becomes more compact when peptide is bound. These changes, which are reflected in peptide-dependent binding of monoclonal antibodies, affect the surfaces of **MHC** molecules available for contact with T cell receptors and hence may influence T cell-receptor recognition of **MHC** molecules.

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Cell Line
Epitopes
Fluorescence
*H-2 Antigens: CH, chemistry
H-2 Antigens: ME, metabolism
Mice
Ovalbumin: ME, metabolism
Peptide. . .

L4 ANSWER 58 OF 82 MEDLINE DUPLICATE 8

AB The T2 mutant cell line is unable to load peptides into the **MHC class I** Ags inside the cells. These "**empty**" **MHC class I** Ags are not expressed on the cell surface unless the cells are cultured at low temperatures. Expression will occur at 37 degrees C only in the presence of peptides that bind to and stabilize the **class I** Ags. T2 cells transfected with the B*2705 gene were tested with a panel of anti-HLA-B27 mAb. Two of the antibodies, ME1 and KS3, reacted with the "**empty**" HLA-B27 expressed at low culture temperatures. Three antibodies, B27.M1, B27.M2, and Ye-2, were unreactive with these "**empty**" HLA-B27. The cells were then incubated with a panel of HLA-B27-binding peptides. One of the antibodies, Ye-2, became reactive when. . .

CT Check Tags: Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antigen-Presenting Cells: IM, immunology
Antigens, Viral: CH, chemistry
Antigens, Viral: IM, immunology
Brefeldin A
. . .

L4 ANSWER 59 OF 82 MEDLINE

TI Protein transfer of preformed **MHC**-peptide complexes sensitizes target cells to T cell cytolysis.

AB . . . a protein transfer vehicle to deliver a hepatitis B virus antigenic peptide to the surfaces of cytotoxic T cell targets. **Empty** HLA-A2.1-GPI/beta 2m was first produced in D. melanogaster cotransfectants and immunoaffinity purified. Cell coating with HLA-A2.1-GPI/beta 2m was shown to. . . presented a hepatitis B virus peptide to peptide-specific HLA-A2.1-restricted T cell clones in cytotoxicity assays. Protein transfer of functional GPI-modified **class I MHC**-antigenic peptide complexes represents a novel strategy for delivering functional antigenic complexes to cell surfaces that bypasses limitations of gene transfer. . .

CT Check Tags: Animal; Human; **Support**, U.S. Gov't, P.H.S.
Antigen Presentation
*Antigen-Presenting Cells: ME, metabolism
Antigen-Presenting Cells: UL, ultrastructure
Cell Line
Cell Membrane: ME, metabolism
*Cytotoxicity,. . .

L4 ANSWER 60 OF 82 MEDLINE

AB Virus-specific cytotoxic T cells recognize antigens in the form of peptides (8 or 9 amino acids long) bound to **MHC class-I** molecules. Exposure of unprimed murine splenocytes to synthetic peptides of viral antigens elicits primary CTL in vitro. The fine specificity of such CTL as well as the correlation between binding affinity of peptides to **class-I** molecules and CTL induction was analysed using synthetic peptides corresponding to overlapping and distinct amino-acid residues in SV40 T antigen. . . naive C57 BL/6 mice. This reactivity was seen regardless of the peptides allelic anchor motifs or their abilities to stabilize **empty**

class-I molecules. However, none of the primary CTL and CTL lines lysed Tag-expressing cells. In contrast, CTL generated in vivo by. . . and were recognized in the context of both Kb and Db molecules. These results have revealed a flexible disposition of MHC class-I molecules with regard to peptide binding and also reflected lack of correlation between binding affinity to class-I molecules and the capacity of peptides to induce primary CTL or to serve as potential targets. The significance of these. . .

CT Check Tags: Animal; Female; Male; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
*Antigens, Polyomavirus Transforming: IM, immunology
Cross Reactions
Cytotoxicity, Immunologic
Histocompatibility Antigens Class I: IM, immunology
Mice
Mice, Inbred C57BL
Molecular Sequence Data
Papovaviridae Infections: IM, immunology
Peptide Fragments: CS,. . .

CN 0 (Antigens, Polyomavirus Transforming); 0 (Histocompatibility Antigens Class I); 0 (Peptide Fragments)

L4 ANSWER 61 OF 82 MEDLINE

TI A quantitative assay to measure the interaction between immunogenic peptides and purified class I major histocompatibility complex molecules.

AB A direct and sensitive biochemical assay to measure the interaction in solution between peptides and affinity-purified major histocompatibility complex (MHC) class I molecules has been generated. Specific binding reflecting the known class I restriction of cytotoxic T cell responses was obtained. Adding an excess of beta 2-microglobulin (beta 2m) significantly increased the rate. . . it did not affect the rate of dissociation. Binding was complicated by a rapid and apparently irreversible loss of functional MHC class I at 37 degrees C which might limit the life span of empty MHC class I thereby preventing the inadvertent exchange of peptides at the target cell surface. All class I molecules tested bound peptides of the canonical octa- to nona-meric length. However, one class I molecule, Kk, also bound peptides, which were much longer suggesting that the preference of class I molecules for short epitopes is not absolute and may be caused by factors other than the peptide-MHC class I binding event itself.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Amino Acid Sequence
*Antigens, Viral: CH, chemistry
Antigens, Viral: ME, metabolism
Binding, Competitive
Cell Line
***Histocompatibility Antigens Class I: ME, metabolism**
Mice
Mice, Inbred AKR
Mice, Inbred BALB C
Mice, Inbred C57BL
Molecular Sequence Data
Peptides:. . .

CN 0 (Antigens, Viral); 0 (Histocompatibility Antigens Class I); 0 (Peptides); 0 (beta 2-Microglobulin)

L4 ANSWER 62 OF 82 MEDLINE

TI Phosphatidyl inositol-linked forms of a murine class I MHC molecule expressed on Chinese hamster ovary cells retain peptide binding capability and alloreactivity.

AB A gene encoding a phosphatidyl inositol-linked form of the murine class I MHC molecule H-2Kd was constructed and the protein expressed in Chinese hamster ovary cells together with murine or human beta 2-microglobulin (beta 2m). The resulting lipid-linked class I heterodimers can be efficiently converted into a soluble form by treatment of transfected cells with a phospholipase. Cells expressing Kd. . . peptide, although more peptide bound to cells expressing the Kd/human beta 2m combination, perhaps because of a greater number of empty molecules at the cell surface. A dissociation constant of 5 x 10(-8) M derived by Scatchard analysis is within the range expected for interactions of peptides with class I MHC molecules. Alloreactive cytotoxic T cells which recognize wild-type Kd on murine cells lysed the hamster cells expressing lipid-linked Kd without. . .

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
CHO Cells
Cytotoxicity Tests, Immunologic
Flow Cytometry
H-2 Antigens: CH, chemistry
*H-2 Antigens: IM,. . .

L4 ANSWER 63 OF 82 MEDLINE

AB . . . is now feasible in experimental murine systems. These CTL recognize peptide sequences of defined length presented by major histocompatibility complex (MHC) class I molecules. Effective eradication of large tumour masses requires co-administration of interleukin 2. Tumour escape strategies are numerous but in various. . . The steps proposed include: (1) identification of target molecules of choice. (2) Identification in these target molecules of peptides fitting MHC allele-specific peptide motifs involved in peptide binding to MHC molecules. (3) Evaluation of actual binding of such peptides to specific MHC class I molecules. (4) In vitro CTL response induction by such peptides, presented by highly efficient antigen-presenting cells such as antigen processing-defective cells carrying empty MHC class I molecules loaded with a single peptide or dendritic cells. Both types of cells are capable of primary CTL response induction. . .

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
*Antigens, Viral: IM, immunology
Cervix Neoplasms: PC, prevention & control
***Histocompatibility Antigens Class I: IM, immunology**
*Immunodominant Epitopes: IM, immunology
*Immunotherapy, Adoptive

Mice
Molecular Sequence Data
*Peptides: IM, immunology
*T-Lymphocytes, Cytotoxic:. . .
CN 0 (Antigens, Viral); 0 (Histocompatibility Antigens **Class** I); 0 (Immunodominant Epitopes); 0 (Peptides)

L4 ANSWER 64 OF 82 MEDLINE
AB Many mouse and human tumours express major histocompatibility complex (**MHC**) **class** I-associated antigens that constitute targets for syngeneic cytotoxic T lymphocytes (CTL). Genes encoding such antigens were isolated from a mouse mastocytoma and from human melanomas by genetic methods. Isolation and characterization of **MHC class** I-associated peptides has enabled specific anchor residues to be identified that are typical of peptides that bind to distinct **class** I molecules. Moreover, CTL specific to particular **MHC**-peptide combinations have been used to identify naturally occurring antigenic peptides in cell extracts and enabled them to be sequenced directly. Most known **MHC** ligands are of viral origin or are self peptides derived from normal proteins. Here we use total acid extraction and. . . carcinoma (3LL)-specific peptide(s), which shows sequence homology to the connexin 37 protein. Synthetic octamers based on these sequences bind to '**empty**' H-2Kb molecules on RMA-S cells, sensitize RMA-S cells to lysis by specific anti-3LL CTL, and induce anti-tumour CTL. The tumour-associated. . .
CT Check Tags: Animal; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, Non-P.H.S.; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antigens, Neoplasm: AN, analysis
*Antigens, Neoplasm: IM, immunology
Connexins: IM, immunology
H-2 Antigens: IM,. . .

L4 ANSWER 65 OF 82 MEDLINE
AB Although it is clear that each component of the **class** I **MHC** trimolecular complex (heavy chain, beta 2m, and antigenic peptide) contributes to its formation and stability, the specific interaction governing assembly. . . using purified H-2Db molecules, we used a solid-phase binding assay recently developed in our laboratory to quantify kinetic parameters for **class** I assembly and disassembly. It was found that the influenza NP peptide Y367-374 associated with preformed **empty** complexes of 28-14-8S- (i.e., anti-alpha 3) bound Db beta 2m dimers much more quickly (t 1/2 < 0.2 h at. . . thermal disassembly (as measured by loss of the B22 epitope, t1/2 2h, 37 degrees C) than the Db beta 2m **empty** dimer (t1/2 0.2 h). Finally, stability of the preformed trimolecular complex of heavy chain, beta 2m, and peptide was found. . .
CT Check Tags: Animal; In Vitro; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Antigens, Viral: CH, chemistry
*Antigens, Viral: ME, metabolism
Epitopes
*H-2 Antigens: ME, metabolism
Influenza A. . .

L4 ANSWER 66 OF 82 MEDLINE DUPLICATE 9
AB In an effort to examine the peptide binding properties of purified **class** I **MHC** molecules, we have developed a solid phase, radiolabeled peptide binding assay based on the use of H-2Db molecules bound to agarose **beads** via heavy chain-specific mAb. Using purified Db beta 2m, recovered from RMA-S cells and bound to immunoadsorbent **beads** through either alpha 1 or alpha 3 region specific antibodies, complete occupancy of these molecules could be achieved with 125I-Y366-374. . . nucleoprotein peptide under the same conditions. When free Db heavy chains were isolated from beta 2m negative R1E.Db cells by **bead**-bound alpha 3-region specific antibody (28-14-8S) and were incubated with human beta 2m, high affinity (Kd 10(-8) M) binding sites were. . . in a beta 2m-reactive form, the R1E.Db cells provide an alternate approach to that of RMA-S derived Db beta 2m **empties** for the creation of homogeneous complexes of Db, beta 2m, and antigenic peptide. We anticipate that these **bead**-bound **empty** and defined peptide-**class** I complexes may be useful in the further study of **class** I **MHC** target structure formation and recognition.
CT Check Tags: Animal; Human; In Vitro; **Support**, Non-U.S. Gov't
Amino Acid Sequence
*Antigens, Viral: ME, metabolism
Gene Products, gag: IM, immunology
*H-2 Antigens: ME, metabolism
HIV-1: IM,. . .

L4 ANSWER 67 OF 82 MEDLINE
TI Reduced expression of major histocompatibility complex **class** I free heavy chains and enhanced sensitivity to natural killer cells after incubation of human lymphoid lines with beta 2-microglobulin.
AB Enhancement of major histocompatibility complex (**MHC**) **class** I expression leads to protection from recognition by natural killer (NK) cells in several systems. **MHC class** I gene products can be expressed in different forms at the cell surface--for example as "**empty**" beta 2-microglobulin (beta 2m)-associated heterodimers or free heavy chains. To study the role of different **class** I heavy chain forms in NK target interactions, we have used lymphoblastoid target cell lines preincubated with beta 2m. This was. . . non-associated--heavy chains in favor of the former. In parallel, there was a significant increase in NK sensitivity. The recognition of **MHC class** I -deficient cell lines was not affected by beta 2m, arguing against a general nonspecific effect of beta 2m on NK sensitivity.. . .
CT Check Tags: Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Cell Line
Epitopes: AN, analysis
Histocompatibility Antigens Class I: AN, analysis
Histocompatibility Antigens Class I: IM, immunology
***Histocompatibility Antigens Class I: PH, physiology**
*Killer Cells, Natural: IM, immunology
*beta 2-Microglobulin: PD, pharmacology
CN 0 (Epitopes); 0 (Histocompatibility Antigens **Class** I); 0 (beta 2-Microglobulin)

L4 ANSWER 68 OF 82 MEDLINE
TI Real-time measurement of antigenic peptide binding to **empty** and preloaded single-chain major histocompatibility complex **class**

I molecules.
AB Cytotoxic T lymphocytes (CTL) recognize peptides in association with major histocompatibility complex (**MHC**) **class I** proteins, but how peptides bind to **class I** is not well understood. We used a fluorescence technique to measure antigenic peptide binding to a soluble, single-chain Kd (SC-Kd). . . . could be followed by monitoring the fluorescence at 530 nm. The dansylated Plasmodium berghei circumsporozoite (PbCS) 263-260 peptide bound to "**empty**" SC-Kd with an association rate constant of 1140 M-1s-1, and the subsequent spontaneous dissociation of the SC-Kd-peptide complex was slow.. . .
CT Check Tags: Human; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Fluorescence
H-2 Antigens: ME, metabolism
***Histocompatibility Antigens Class I: ME, metabolism**
Hydrogen-Ion Concentration
Kinetics
Molecular Sequence Data
*Peptide Fragments: ME, metabolism
T-Lymphocytes, Cytotoxic: IM, immunology
Temperature
CN 0 (H-2 Antigens); 0 (H-2K(K) antigen); 0 (Histocompatibility Antigens **Class I**); 0 (Peptide Fragments)

L4 ANSWER 69 OF 82 MEDLINE
TI Thermal stability comparison of purified **empty** and peptide-filled forms of a **class I MHC** molecule.
AB A secreted form of a **class I** major histocompatibility complex (**MHC**) molecule was denatured and renatured in vitro in the absence of peptide. The resulting **empty class I** heterodimer was immunologically reactive and structurally similar to a heterodimer renatured in the presence of an appropriate restricted peptide. Thermal. . . the two forms of heterodimer differed in their resistance to denaturation by heat but that a significant portion of the **empty class I** heterodimers had a native conformation at physiological temperatures. Free energies calculated from these data gave a direct measure of the stabilization of the **class I MHC** molecule that resulted from peptide binding.
CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
CHO Cells
Circular Dichroism
Drug Stability
Enzyme-Linked Immunosorbent Assay
Glutamate-Ammonia Ligase: GE, genetics
Glutamate-Ammonia Ligase: ME, metabolism
Hamsters
Heat
***Histocompatibility Antigens Class I: CH, chemistry**
***Histocompatibility Antigens Class I: GE, genetics**
Macromolecular Systems
*Protein Conformation
Protein Folding
Thermodynamics
Transfection
CN 0 (Histocompatibility Antigens **Class I**); 0 (Macromolecular Systems); EC 6.3.1.2 (Glutamate-Ammonia Ligase)

L4 ANSWER 70 OF 82 MEDLINE
AB Serologically distinct forms of H-2Kb are stabilized by loading cells expressing "**empty**" **class I** major histocompatibility complex (**MHC**) molecules with different H-2Kb binding peptides. The H-2Kb epitope recognized by monoclonal antibody (mAb) 28.8.6 was stabilized by ovalbumin (OVA). . . partially stabilized by substitution of the third or the fifth residues in the peptides. These results indicate that distinct conformational **MHC** epitopes are dependent on the specific peptide that occupies the antigenic peptide binding groove on individual **MHC** molecules. The changes in **MHC** epitopes observed may also be important in understanding the diversity of T cell receptors used in an immune response and. . .
CT Check Tags: Animal; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Amino Acid Sequence
Antibodies, Monoclonal
Cell Line
Cell Membrane: IM, immunology
*Epitopes: CH, chemistry
Epitopes: IM, immunology
. . .

L4 ANSWER 71 OF 82 MEDLINE
AB The identification of naturally processed viral peptides reveals that major histocompatibility complex (**MHC**) **class I** epitopes are composed of nine or eight amino acid residues. Peptides eluted from H-2 Kb **MHC class I** molecules have been suggested, as a class, to be eight amino acid residues long. To assay for peptide-**class I** interactions, a stabilization assay described for surface labeled "**empty**" **class I** molecules was employed, but on biosynthetically labeled **class I** molecules. The Sendai virus nucleoprotein-derived octapeptide APGNYPAL does not bind and stabilize Kb molecules, whereas other octameric Kb-restricted peptides and. . . significantly alters the binding properties of the nonamer peptide. We conclude that the length of epitopes as selected by the **class I** Kb molecule is influenced by their sequence and suggest that proper positioning of the NH2 terminus of peptides is essential for **class I** stabilizing properties. The ability to stabilize newly synthesized "**empty**" **class I** molecules with peptide argues against an involvement of beta 2 microglobulin exchange in the experiments described here.
CT Check Tags: Animal; **Support**, Non-U.S. Gov't
Amino Acid Sequence
*Antibody Specificity: GE, genetics
Antigen-Antibody Reactions
Cell Line
Chromatography, Thin Layer
Electrophoresis
Epitopes: GE, genetics
. . .

L4 ANSWER 72 OF 82 MEDLINE

AB Several trinitrophenyl (TNP)-specific mouse cytotoxic T cell (CTL) clones recognize TNP-conjugated peptides in association with **class I MHC** molecules ('hapten-peptide determinants'). However, cell modification with trinitrobenzene sulfonic acid (TNBS) also leads to the formation of TNP determinants covalently attached to **MHC** molecules ('altered self'). To determine the importance of 'peptide' versus 'altered self' determinants, we used the mutant cell line RMA-S which expresses peptide-free ('**empty**') Kb and Db molecules at 26 degrees C. Additionally, we stabilized Kb molecules on RMA-S cells at 37 degrees C. . . . recognized TNP self-peptides extracted from TNBS-treated syngeneic spleen cells. Taken together, these data clearly show that TNP residues linked to **MHC** via associated peptides but not by covalent bondage represent the dominant antigenic epitopes for **class I MHC**-restricted, hapten-specific T cells.

CT Check Tags: Animal; In Vitro; **Support**, Non-U.S. Gov't
Amino Acid Sequence
Clone Cells
Cytotoxicity, Immunologic
Epitopes
Haptens
Histocompatibility Antigens Class I: IM, immunology
Mice
Mice, Inbred C57BL
Molecular Sequence Data
Peptides: CH, chemistry
Peptides: IM, immunology
*T-Lymphocytes,. . .

CN 0 (Epitopes); 0 (Haptens); 0 (Histocompatibility Antigens **Class I**); 0 (Peptides); 0 (Trinitrobenzenes)

L4 ANSWER 73 OF 82 MEDLINE

AB The mutant human cell line T2 is defective in antigen presentation in the context of **class I** major histocompatibility complex (**MHC**) molecules, and also in that transfected T2 cells show poor surface expression of exogenous human **class I** (HLA) alleles. Both defects are thought to lie in the transport of antigenic peptides derived from cytosolic proteins into the endoplasmic reticulum (ER), as peptide-deficient **class I** molecules might be expected to be either unstable or retained in the ER. The products of several mouse **class I** (H-2) genes, and the endogenous gene HLA-A2 do, however, reach the surface of T2 cells at reasonable levels although they. . . HLA molecules do not significantly bind endogenous peptides. Surprisingly, H-2 molecules expressed in T2 also lack associated peptides, arguing that '**empty**' complexes of mouse **class I** glycoproteins with human beta 2-microglobulin are neither retained in the ER nor unstable. HLA-A2 molecules, however, do bind high levels. . .

CT Check Tags: Human; **Support**, U.S. Gov't, P.H.S.
Alleles
Amino Acid Sequence
Cell Line
Cell Membrane: IM, immunology
***Genes, MHC Class I**
*HLA Antigens
HLA-A Antigens: GE, genetics
HLA-A Antigens: IP, isolation & purification
*HLA-A2 Antigen: GE, genetics
HLA-B. . .

L4 ANSWER 74 OF 82 MEDLINE

TI The role of beta-2 microglobulin in temperature-sensitive and interferon-gamma-induced exocytosis of HLA **class I** molecules.

AB The passage of **MHC class I** heavy chains through the exocytic pathway is promoted by association with beta 2 microglobulin (beta 2m). In order to analyze the structural basis of this phenomenon, processing and cell surface expression of HLA **class I** molecules have been investigated in the beta 2m null human melanoma cell line FO-1 transfected with either the human or. . . transfectant of the FO-1 cell line (designated FO-1H), FO-1 cells transfected with the mouse beta 2m gene (FO-1C) express HLA **class I** molecules that are processed with grossly altered kinetics and are present on the cell surface at reduced levels. The suboptimal expression of HLA **class I** heavy chains encoded by FO-1C cells reflects a defect in heavy chain stability since cell surface expression of HLA **class I** antigens was increased following incubation at 30 degrees C. The increased cell surface expression paralleled accelerated processing of HLA **class I** heavy chains by FO-1C cells. In contrast, no induction in either cell surface expression or processing of HLA **class I** heavy chains was observed for the beta 2m-negative FO-1 parent cell line, which remained HLA **class I** antigen null when cultured at 30 degrees C, or the FO-1H human beta 2m transfectant, which expressed equivalent levels of HLA **class I** antigens on the cell surface at 37 degrees C and 30 degrees C. Further up-regulation of the temperature-sensitive induction of HLA **class I** antigen expression was accomplished by treatment of the FO-1C transfectant with interferon-gamma; this latter effect appears to be active at. . . potent a transcriptional activator at 30 degrees C as it was at 37 degrees C. These results indicate that HLA **class I** heavy chains expressed by FO-1C cells are subject to temperature-sensitive and cytokine-inducible stabilization that increases their affinity for the structural variant of beta 2m and promotes exocytosis of the HLA **class I** heterodimer to the cell surface. Furthermore, beta 2m non-conformed **MHC class I** heavy chains undergo stabilization that is not associated with enhanced cell surface expression, indicating that the exocytosis of putative " **empty**" HLA **class I** antigens is a process dependent upon association with beta 2m.

CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
Base Sequence
*Exocytosis: DE, drug effects
***Histocompatibility Antigens Class I: PH, physiology**
*Interferon Type II: PD, pharmacology
Melanoma
Mice
Molecular Sequence Data
Temperature
Transfection
Tumor Cells, Cultured:. . .

CN 0 (Histocompatibility Antigens **Class I**); 0 (beta

2-Microglobulin)

L4 ANSWER 75 OF 82 MEDLINE
AB . . . now feasible in experimental murine systems. These CTL recognize viral peptide sequences of defined length presented in the groove of **MHC class I** molecules. Effective eradication of large tumour masses requires coadministration of IL-2. In essence, T cell immunity against virus induced tumours. . . . products. The various steps proposed include: (a) identification of target molecules of choice; (b) identification in these target molecules of **MHC** allele specific peptide motifs involved in peptide binding to **MHC** molecules; (c) evaluation of actual binding of such peptides to specific **MHC class I** molecules; (d) in vitro CTL response induction by such peptides, presented either by highly efficient antigen presenting cells (such as processing defective cells, which carry **empty MHC class I** molecules) loaded with a single peptide or by dendritic cells, both cell types being capable of primary CTL response induction. . .
CT Check Tags: Animal; Human; **Support**, Non-U.S. Gov't
Immunologic Surveillance: IM, immunology
Immunotherapy, Adoptive
*Lymphoma: IM, immunology
Lymphoma: TH, therapy
*Neoplasms: IM, immunology
Neoplasms: TH, therapy
. . .

L4 ANSWER 76 OF 82 MEDLINE
TI Peptide loading of **empty** major histocompatibility complex molecules on RMA-S cells allows the induction of primary cytotoxic T lymphocyte responses.
AB The antigen processing-defective mutant cell line RMA-S expresses at the cell surface major histocompatibility complex (**MHC**) **class I** molecules devoid of peptide that can be efficiently loaded with exogenous immunogenic peptides. We now report that viral peptide-loaded RMA-S. . . virus-infected cells. Pre-culture of RMA-S cells at low temperature (22 degrees - 26 degrees C), which increases the amount of **empty MHC class** I molecules at the cell surface, decreases the peptide concentrations required for the induction of primary CTL responses. Primary peptide-specific CTL responses induced by peptide-loaded RMA-S cells are CD4+ cell- and **MHC** class II+ cell-independent. CTL response induction is blocked by the presence of anti-CD8 monoclonal antibody during culture. Direct peptide binding studies confirm the efficient loading of **empty MHC** molecules on RMA-S cells with peptide and show 2.5-fold more peptide bound per RMA-S cell compared to RMA cells. An. . . the difference in primary response induction between RMA and RMA-S cells is related to the CD8 dependence of these responses. **MHC class I** molecules occupied with irrelevant peptides (a majority present on RMA, largely absent on RMA-S) may interfere in the interaction of the CD8 molecule with relevant **MHC**/peptide complexes. The results delineate a novel strategy of peptide based in vitro immunization to elicit CD8+ cytotoxic T cell responses.
CT Check Tags: Animal; In Vitro; **Support**, Non-U.S. Gov't
Adenoviridae: IM, immunology
Amino Acid Sequence
*Antigens, Viral: CH, chemistry
Cell Line
Cytotoxicity, Immunologic
*H-2 Antigens: ME, metabolism
. . .

L4 ANSWER 77 OF 82 MEDLINE DUPLICATE 10
TI Exogenous beta 2-microglobulin is required for antigenic peptide binding to isolated **class I** major histocompatibility complex molecules.
AB Binding of antigenic peptides to purified **class I** major histocompatibility complex (**MHC**) molecules, as measured by antigen-specific cytolytic T lymphocyte (CTL) degranulation, was found to occur in the presence of serum but not in its absence. The role of soluble beta 2-microglobulin (beta 2m), a normal component of serum, in **class I**-peptide complex formation was therefore examined. Sera depleted of beta 2m did not **support** effective peptide binding to **class I**, but binding was restored in the presence of low concentrations of purified human beta 2m. Sequential incubation of immobilized **class I** with human beta 2m first, followed by peptide, resulted in antigenic complex formation, while reversing the order of pulsing could. . . results were obtained in experiments examining H-2Db, Kb and Kd with appropriate peptides and CTL. These results demonstrate that mature **class** I proteins are not able to directly bind peptide, but that interaction with exogenous beta 2m results in a structure that will subsequently bind peptide. Binding of exogenous beta 2m appears to result in "**empty**" **class I** molecules, possibly by exchange for endogenous beta 2m, with a concomitant loss of endogenous peptide.
CT Check Tags: Animal; In Vitro; **Support**, Non-U.S. Gov't; **Support**, U.S. Gov't, P.H.S.
*Antigen-Antibody Reactions: PH, physiology
Cell Degranulation: IM, immunology
Cell Line
H-2 Antigens: ME, metabolism
***Histocompatibility Antigens Class I: ME, metabolism**
Mice
T-Lymphocytes, Cytotoxic: IM, immunology
*beta 2-Microglobulin: PD, pharmacology
CN 0 (H-2 Antigens); 0 (H-2K(K) antigen); 0 (H-2k(b) antigen); 0 (Histocompatibility Antigens **Class I**); 0 (beta 2-Microglobulin); 0 (histocompatibility antigen H-2D(b))

L4 ANSWER 78 OF 82 MEDLINE
TI Peptide selection by **MHC class I** molecules.
AB . . . in specific cases, truncations of peptides improves sensitization of target cells, no optimum length for binding to major histocompatibility complex (**MHC**) **class I** molecules has been defined. We have now analysed synthetic peptide captured by **empty MHC class I** molecules of the mutant cell line RMA-S. We found that **class I** molecules preferentially bound short peptides (nine amino acids) and selectively bound these peptides even when they were a minor component. . .
CT Check Tags: Animal; **Support**, Non-U.S. Gov't
Amino Acid Sequence

Cell Line
Cell Transformation, Neoplastic
Epitopes: AN, analysis
Epitopes: IM, immunology
*Histocompatibility Antigens Class I: IM, immunology
Mice
Molecular Sequence Data
Oligopeptides: CS, chemical synthesis
Oligopeptides: IM, immunology
Protein Binding
Rauscher Virus:. . .
CN 0 (Epitopes); 0 (Histocompatibility Antigens Class I);
0 (Oligopeptides)

L4 ANSWER 79 OF 82 MEDLINE
TI Fine peptide specificity of cytotoxic T lymphocytes directed against adenovirus-induced tumours and peptide-MHC binding.
AB . . . mutant peptides were still recognized by an Ad5-specific CTL clone and which deletion mutant peptides still bound to major histocompatibility-complex (MHC) class-I molecules. Binding was analyzed with RMA-S cells that express largely empty and unstable MHC-class-I molecules which are stabilized by peptide binding. We show here that flanking an 8 mer aa sequence, originally described by us as the minimal epitope recognized by CTL, 2 additional aa are important for MHC binding. This leads to the conclusion that this 10-mer peptide is optimal for MHC binding and T-cell recognition. Areas of the peptide primarily involved in binding to MHC or in T-cell recognition are delineated.
CT Check Tags: Animal; Support, Non-U.S. Gov't
*Adenoviruses, Human: GE, genetics
Amino Acid Sequence
Binding Sites
Cell Line
*Cell Transformation, Neoplastic
Chromosome Deletion
*Cytotoxicity, Immunologic
Embryo
*H-2 Antigens: GE, genetics
Histocompatibility Antigens Class I: GE, genetics
*Histocompatibility Antigens Class I: IM, immunology
Mice
Molecular Sequence Data
Peptides: CS, chemical synthesis
*Peptides: IM, immunology
*T-Lymphocytes, Cytotoxic: IM, immunology
CN 0 (H-2 Antigens); 0 (Histocompatibility Antigens Class I
); 0 (Peptides)

L4 ANSWER 80 OF 82 MEDLINE
TI Excess beta 2 microglobulin promoting functional peptide association with purified soluble class I MHC molecules.
AB T lymphocytes expressing alpha beta receptors recognize antigenic peptide fragments bound to major histocompatibility complex class I or class II molecules present on the surface membranes of other cells. Peptide fragments are present in the two available HLA crystal structures and recent data indicate that peptide is required for the stable folding of the class I heavy chain and maintenance of its association with the class I light chain, beta 2-microglobulin (beta 2m), at physiological temperature. To explain how the exogenous peptide used to create targets for cytotoxic cells bearing CD8 antigen could associate with apparently peptide-filled extracellular class I molecules, we hypothesized that stable binding of exogenous peptide to mature class I molecules reflects either the replacement of previously bound peptide during the well documented beta 2m exchange process or the loading of ' empty' class I heavy chains dependent on the availability of excess beta 2m. In either case, free beta 2m should enhance peptide/class I binding. Using either isolated soluble class I molecules or living cells, we show here that free purified beta 2m markedly augments the generation of antigenic complexes capable. . .
CT Check Tags: Human; Support, Non-U.S. Gov't
Cell-Free System
*Gene Products, env: ME, metabolism
HIV Envelope Protein gp160
*HLA Antigens: ME, metabolism
Hybridomas: ME, metabolism
. . .

L4 ANSWER 81 OF 82 MEDLINE
TI Direct binding of peptide to empty MHC class I molecules on intact cells and in vitro.
AB MHC class I molecules devoid of peptide are expressed on the cell surface of the mouse mutant lymphoma cell line RMA-S upon culture at reduced temperature. Empty class I molecules are thermolabile at the cell surface and in detergent lysates, but can be stabilized by the addition of presentable peptide; peptide binding appears to be a rapid process. Furthermore, class I molecules on the surface of RMA-S (H-2b haplotype) cells cultured at 26 degrees C can efficiently and specifically bind iodinated. . . cells (RMA) cultured at 26 degrees C. These experiments underscore the role for peptide in maintenance of the structure of class I molecules and, more importantly, provide two assay systems to study the interactions of peptides with MHC class I molecules independent of the availability of T cells that recognize a particular peptide-MHC class I complex.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Cell Line
Cell Membrane: IM, immunology
Electrophoresis, Polyacrylamide Gel
H-2 Antigens: IM, immunology
*Histocompatibility Antigens Class I: IM, immunology
Histocompatibility Antigens Class I: IP, isolation & purification
Immunoenzyme Techniques
Mice
Peptides: CS, chemical synthesis
Protein Binding
CN 0 (H-2 Antigens); 0 (Histocompatibility Antigens Class I
); 0 (Peptides)

L4 ANSWER 82 OF 82 MEDLINE

TI Empty MHC class I molecules come out in the cold.

AB Major histocompatibility complex (MHC) class I molecules present antigen by transporting peptides from intracellularly degraded proteins to the cell surface for scrutiny by cytotoxic T cells. Recent work suggests that peptide binding may be required for efficient assembly and intracellular transport of MHC class I molecules, but it is not clear whether class I molecules can ever assemble in the absence of peptide. We report here that culture of the murine lymphoma mutant cell. . . . exposure to specific peptides known to interact with H-2Kb or Db. Our findings suggest that, in the absence of peptides, class I molecules can assemble but are unstable at body temperature. The induction of such molecules at reduced temperature opens new ways to analyse the nature of MHC class I peptide interactions at the cell surface.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.
Antigen-Presenting Cells: IM, immunology
Biological Transport
Cell Membrane: IM, immunology
*Cold
H-2 Antigens: IM, immunology
*H-2 Antigens:. . .

=> dis his

(FILE 'HOME' ENTERED AT 12:52:53 ON 16 APR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 12:53:02 ON 16 APR 2002
L1 41486 S (MHC AND (CLASS (1N) I))
L2 374 S L1 AND EMPTY
L3 106 S L2 AND (SUPPORT OR MATRIX OR BEAD)
L4 82 DUP REM L3 (24 DUPLICATES REMOVED)
L5 24364 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER ?/AU
L6 7162 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER P?/AU
L7 8 S L6 AND (MHC AND EMPTY)
L8 5 DUP REM L7 (3 DUPLICATES REMOVED)

=> s l2 and (bead or sepharose)
L9 5 L2 AND (BEAD OR SEPHAROSE)

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 2 DUP REM L9 (3 DUPLICATES REMOVED)

=> dis l10 ibib abs kwic

L10 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:490904 BIOSIS
DOCUMENT NUMBER: PREV199800490904
TITLE: Secondary structure composition and pH-dependent conformational changes of soluble recombinant HLA-DM.
AUTHOR(S): Busch, Robert (1); Reich, Ziv; Zaller, Dennis M.; Sloan, Victor; Mellins, Elizabeth D.
CORPORATE SOURCE: (1) Dep. Pediatr., Stanford Univ. Med. Cent., 300 Pasteur Dr., Stanford, CA 94305-5208 USA
SOURCE: Journal of Biological Chemistry, (Oct. 16, 1998) Vol. 273, No. 42, pp. 27557-27564.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English

AB HLA-DM catalyzes the release of invariant chain fragments from newly synthesized major histocompatibility complex (MHC) class II molecules, stabilizes empty class II molecules, and edits class II-associated peptides by preferentially releasing those that are loosely bound. The ability of HLA-DM to carry out these functions in vitro is pH dependent, with an optimum at pH 4.5-5.5 and poor activity at pH 7. The structural basis for these properties of HLA-DM is unknown. Sequence homology suggests that HU-DM resembles classical, peptide-binding MHC class II molecules. In this study, we examined whether HLA-DM has a secondary structure composition consistent with an MHC fold and whether HLA-DM changes conformation between pH 5 and pH 7. Far-UV circular dichroism (CD) spectra of recombinant soluble HLA-DM (sDM) indicate that HLA-DM belongs to the alpha/beta class of proteins and structurally resembles both MHC class I and class II molecules. The CD peak around 198 nm increases upon going from neutral to endosomal pH and drops sharply upon denaturation below pH 3.5, distinguishing at least three states of sDM. the denatured state and two highly similar folded states. Fluorescence emission spectra show a slight blue-shift and a apprx20% drop in intensity at pH 5 compared with pH 7. Unfolding experiments using guanidinium chloride show that the stability of sDM is somewhat reduced but not lost at pH 5. These results indicate that sDM undergoes a pH-dependent conformational change between neutral and endosomal pH. The change seems to involve both hydrogen bonding patterns and the hydrophobic core of sDM and may contribute to the pH dependence of DM activity.

AB HLA-DM catalyzes the release of invariant chain fragments from newly synthesized major histocompatibility complex (MHC) class II molecules, stabilizes empty class II molecules, and edits class II-associated peptides by preferentially releasing those that are loosely bound. The ability of HLA-DM. . . pH 7. The structural basis for these properties of HLA-DM is unknown. Sequence homology suggests that HU-DM resembles classical, peptide-binding MHC class II molecules. In this study, we examined whether HLA-DM has a secondary structure composition consistent with an MHC fold and whether HLA-DM changes conformation between pH 5 and pH 7. Far-UV circular dichroism (CD) spectra of recombinant soluble HLA-DM (sDM) indicate that HLA-DM belongs to the alpha/beta class of proteins and structurally resembles both MHC class I and class II molecules.
The CD peak around 198 nm increases upon going from neutral to endosomal pH and drops sharply upon. . .

IT . . .
CB, purification method; far-UV circular dichroism spectroscopy: analytical method, spectroscopic techniques: CB; fluorescence spectroscopy: analytical method, spectroscopic techniques: CB; glycine-coupled CNBr-Sepharose column: laboratory equipment; immunoaffinity chromatography: Recombinant Protein Protocols, purification method, affinity chromatography; Aviv 62DS spectropolarimeter: laboratory equipment; Hitachi F-4010 spectrofluorimeter:. . .

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<------User Break------>
u
=> dis l10 1-2 ibib abs kwic

L10  ANSWER 1 OF 2  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:   1998:490904  BIOSIS
DOCUMENT NUMBER:    PREV199800490904
TITLE:              Secondary structure composition and pH-dependent
                    conformational changes of soluble recombinant HLA-DM.
AUTHOR(S):          Busch, Robert (1); Reich, Ziv; Zaller, Dennis M.; Sloan,
                    Victor; Mellins, Elizabeth D.
CORPORATE SOURCE:   (1) Dep. Pediatr., Stanford Univ. Med. Cent., 300 Pasteur
                    Dr., Stanford, CA 94305-5208 USA
SOURCE:             Journal of Biological Chemistry, (Oct. 16, 1998) Vol. 273,
                    No. 42, pp. 27557-27564.
                    ISSN: 0021-9258.
DOCUMENT TYPE:      Article
LANGUAGE:           English
AB   HLA-DM catalyzes the release of invariant chain fragments from newly
     synthesized major histocompatibility complex (MHC) class II
     molecules, stabilizes empty class II molecules, and edits class
     II-associated peptides by preferentially releasing those that are loosely
     bound. The ability of HLA-DM to carry out these functions in vitro is pH
     dependent, with an optimum at pH 4.5-5.5 and poor activity at pH 7. The
     structural basis for these properties of HLA-DM is unknown. Sequence
     homology suggests that HU-DM resembles classical, peptide-binding
     MHC class II molecules. In this study, we examined whether HLA-DM
     has a secondary structure composition consistent with an MHC
     fold and whether HLA-DM changes conformation between pH 5 and pH 7. Far-UV
     circular dichroism (CD) spectra of recombinant soluble HLA-DM (sDM)
     indicate that HLA-DM belongs to the alpha/beta class of proteins and
     structurally resembles both MHC class I and
     class II molecules. The CD peak around 198 nm increases upon going
     from neutral to endosomal pH and drops sharply upon denaturation below pH
     3.5, distinguishing at least three states of sDM. the denatured state and
     two highly similar folded states. Fluorescence emission spectra show a
     slight blue-shift and a apprx20% drop in intensity at pH 5 compared with
     pH 7. Unfolding experiments using guanidinium chloride show that the
     stability of sDM is somewhat reduced but not lost at pH 5. These results
     indicate that sDM undergoes a pH-dependent conformational change between
     neutral and endosomal pH. The change seems to involve both hydrogen
     bonding patterns and the hydrophobic core of sDM and may contribute to the
     pH dependence of DM activity.
AB   HLA-DM catalyzes the release of invariant chain fragments from newly
     synthesized major histocompatibility complex (MHC) class II
     molecules, stabilizes empty class II molecules, and edits class
     II-associated peptides by preferentially releasing those that are loosely
     bound. The ability of HLA-DM.  .  .  pH 7. The structural basis for these
     properties of HLA-DM is unknown. Sequence homology suggests that HU-DM
     resembles classical, peptide-binding MHC class II molecules. In
     this study, we examined whether HLA-DM has a secondary structure
     composition consistent with an MHC fold and whether HLA-DM
     changes conformation between pH 5 and pH 7. Far-UV circular dichroism (CD)
     spectra of recombinant soluble HLA-DM (sDM) indicate that HLA-DM belongs
     to the alpha/beta class of proteins and structurally resembles both
     MHC class I and class II molecules.
     The CD peak around 198 nm increases upon going from neutral to endosomal
     pH and drops sharply upon.  .  .
IT   .  .  .
        CB, purification method; far-UV circular dichroism spectroscopy:
        analytical method, spectroscopic techniques: CB; fluorescence
        spectroscopy: analytical method, spectroscopic techniques: CB;
        glycine-coupled CNBr-Sepharose column: laboratory equipment;
        immunoaffinity chromatography: Recombinant Protein Protocols,
        purification method, affinity chromatography; Aviv 62DS
        spectropolarimeter: laboratory equipment; Hitachi F-4010
        spectrofluorimeter:.  .  .


L10  ANSWER 2 OF 2     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   93389134     MEDLINE
DOCUMENT NUMBER:    93389134   PubMed ID: 8397250
TITLE:              High occupancy binding of antigenic peptides to purified,
                    immunoadsorbed H-2Db beta 2m molecules.
AUTHOR:             Burshtyn D N; Barber B H
CORPORATE SOURCE:   Department of Immunology, University of Toronto, Canada.
SOURCE:             JOURNAL OF IMMUNOLOGY, (1993 Sep 15) 151 (6) 3070-81.
                    Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        199310
ENTRY DATE:         Entered STN: 19931105
                    Last Updated on STN: 19970203
                    Entered Medline: 19931020
AB   In an effort to examine the peptide binding properties of purified
     class I MHC molecules, we have developed a
     solid phase, radiolabeled peptide binding assay based on the use of H-2Db
     molecules bound to agarose beads via heavy chain-specific mAb.
     Using purified Db beta 2m, recovered from RMA-S cells and bound to
     immunoadsorbent beads through either alpha 1 or alpha 3 region
     specific antibodies, complete occupancy of these molecules could be
     achieved with 125I-Y366-374 influenza nucleoprotein peptide (Kd 10(-7) M).
     Approximately 12% of the Db beta 2m dimers recovered from RMA cells could
     be occupied by this influenza nucleoprotein peptide under the same
     conditions. When free Db heavy chains were isolated from beta 2m negative
     R1E.Db cells by bead-bound alpha 3-region specific antibody
     (28-14-8S) and were incubated with human beta 2m, high affinity (Kd 10(-8)
     M) binding sites were created for the 125I-Y367-374 influenza
     nucleoprotein peptide. In addition to demonstrating that a significant
     fraction of the heavy chains present in R1E.Db cells are in a beta
     2m-reactive form, the R1E.Db cells provide an alternate approach to that
     of RMA-S derived Db beta 2m empties for the creation of
     homogeneous complexes of Db, beta 2m, and antigenic peptide. We anticipate
     that these bead-bound empty and defined peptide-
     class I complexes may be useful in the further study of
     class I MHC target structure formation and
     recognition.
AB   In an effort to examine the peptide binding properties of purified
     class I MHC molecules, we have developed a
```

solid phase, radiolabeled peptide binding assay based on the use of H-2Db molecules bound to agarose **beads** via heavy chain-specific mAb. Using purified Db beta 2m, recovered from RMA-S cells and bound to immunoadsorbent **beads** through either alpha 1 or alpha 3 region specific antibodies, complete occupancy of these molecules could be achieved with 125I-Y366-374. . . . nucleoprotein peptide under the same conditions. When free Db heavy chains were isolated from beta 2m negative R1E.Db cells by **bead**-bound alpha 3-region specific antibody (28-14-8S) and were incubated with human beta 2m, high affinity (Kd 10(-8) M) binding sites were. . . . in a beta 2m-reactive form, the R1E.Db cells provide an alternate approach to that of RMA-S derived Db beta 2m **empties** for the creation of homogeneous complexes of Db, beta 2m, and antigenic peptide. We anticipate that these **bead**-bound **empty** and defined peptide-**class** I complexes may be useful in the further study of **class** I **MHC** target structure formation and recognition.

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(FILE 'HOME' ENTERED AT 12:52:53 ON 16 APR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 12:53:02 ON 16 APR 2002

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L1         41486 S (MHC AND (CLASS (1N) I))
L2           374 S L1 AND EMPTY
L3           106 S L2 AND (SUPPORT OR MATRIX OR BEAD)
L4            82 DUP REM L3 (24 DUPLICATES REMOVED)
L5         24364 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER ?/AU
L6          7162 S LUXEMBURG A?/AU OR JACKSON M?/AU OR PETER P?/AU
L7             8 S L6 AND (MHC AND EMPTY)
L8             5 DUP REM L7 (3 DUPLICATES REMOVED)
L9             5 S L2 AND (BEAD OR SEPHAROSE)
L10            2 DUP REM L9 (3 DUPLICATES REMOVED)
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=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

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